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THE IMPORTANCE OF IMMUNE BIOLOGIC PROCESSES IN THE MORPHOLOGY OF SKIN LESIONS *

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Morphology must always be the basis of clinical medicine, but it does not satisfy the desire for causality. In addition to many other advances in the study of endocrine organs, in the sympathetic and parasympathetic nervous systems, in heredity and in medical chemistry, it is immune biologic knowledge in a general sense of the word which has been the principal aid in the understanding of the pathogenesis of skin lesions. The application of this knowledge to morphology not only increases the interest of the clinic in dermatoses, but is also of use in diagnosis and of great heuristic value, especially in those diseases the etiology of which is as yet unknown.

A systematic review of this subject seems to be lacking in the literature. I cannot give such a review here but should like to show roughly that the study of the form of skin lesions has been advanced through immune biology. In this I shall deal mainly with infectious dermatoses, but I shall also briefly mention toxic dermatoses, skin diseases of unknown etiology and even tumors.

The various lesions caused by different infections are nothing other than varying manifestations of the battle between the organism (in this case, the skin) and the microbes.

The absolute number of general pathologic processes which can be caused by living organisms in the skin is limited, and it is astonishing how varied the clinical and histologic manifestations become through the different combinations of these few basic processes. The determining factors for the resulting forms are on the one hand the special properties of the microbes, and on the other hand peculiarities of the skin and of the general organism. With the exception of the brain, there is probably no organ in which individuality dominates the manifestations of disease as noticeably as the skin. The connection between the pathology of the skin and the constitution of the skin and of the organism is still far from completely recognized. Understanding of the forms of skin diseases has been but little advanced through the differentiations of the skin of blonde and brunette, of oily and dry skin, etc., although these conditions are, without a doubt, constitutional peculiarities. The local

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differences of various regions of the skin also play an important rôle in the picture of the disease; e. g., the palms and soles react to the same infection differently than the skin of the torso and the head, and the skin eruptions are very different in their manifestations according to the individual person and disease. Because of the boundaries of the regions of the nerve supply and the hair streams there are differences of the reaction type. Internal and external causes can determine provocation or protection; for example, paralyses, points of pressure, pigment anomalies, effect of light, vasomotor or cyanotic hyperemia, anemia, etc.

It is entirely unknown why certain sites are particularly disposed or immune to a harmful chemical agent (fixed exanthems and refractory zones). This points to analogous influences in infections as well. In addition, perhaps the most important factor is the individually varying possibility of sensitization and desensitization. This varies to the greatest degree and thus leads to the great individual variations in the course of a disease even though the disease is caused by the same bacterial strain and runs its course under identical external conditions; for example, conjugal syphilis or congenital syphilis in brothers, etc. The microbes can change under the influence of the organism (for example, trichophyton fungi when they get into the blood); they can modify their virulence and even their contagiosity in the course of an epidemic (impetigo), and very similar kinds are different from one another in their affinities for the various regions and different tissues of the skin (staphylococci and streptococci).

In spite of the small number of reaction types available, when one considers the great number of variable conditions that exist from disease to disease and from patient to patient, one wonders that the majority of cases still take a typical course. This is why an etiologic diagnosis can generally be made from the clinical picture. This can only be caused by the fact that in both the macro-organism and the micro-organism, those qualities predominate which still keep within certain limits of variation. Through departures from these norms the atypical pictures are produced, and it is natural that under these conditions etiologically different diseases can clinically become confusingly similar (lupus and lupoid syphilis, lichenoid tuberculids and trichophytids). It is just these atypical forms which can be approached through knowledge of immune biologic analogies. In all these cases the question must not be: Is the peculiarity of the harmful agent or the peculiarity of the individual dominant? Instead, each factor must be carefully weighed in each individual case.

Perhaps the importance of immune biology for the development of the lesions becomes clearest when the simplest questions are asked; these are just the questions which are discussed the least because they seem the simplest. That which is taken as self-explanatory is that which is

usually most difficult to explain. I will only mention one of these points, another of which will be treated later on; that is, the spontaneous healing, and particularly the very different individual spontaneous healing, of infectious lesions that have apparently been produced under identical conditions. Various factors here work together—the speed and intensity of defensive forces, in which one must distinguish between the local forces and those of the entire skin and those of the organism as a whole. One must also consider separately the mechanism of these defensive forces (e. g., destruction, and elimination), the growing power of the micro-organism and its variability, again particularly under the influence of the macro-organism.

In order to demonstrate in the clearest possible form, the importance of immune biologic phenomena for the morphology of dermatoses, I will not discuss the different lesions as a whole. Instead, I shall start with one skin disease and then point out the analogies to and differences from the others.

Tricophytic diseases are those dermatoses which are best studied by means of immune biology. The pictures which have been especially found in the so-called deep forms (Bloch and many other writers) are familiar. The strains of fungi causing them come from animals and are very virulent for human beings. Particularly on the scalp and beard, after penetrating the follicular apparatus, they cause acute suppurating inflammation with destruction of the follicle and the formation of granulation tissue. In these cases the skin of the entire body becomes allergic to trichophytin. One can conclude from experiments on animals that this allergy is already the cause of the acute local reaction. The same fungus infecting skin with only the lanugo hairs generally causes only superficial and not suppurating and granulating inflammation and no demonstrable allergy to tricophytin. This contrast is probably caused by the fact that these fungi meet conditions in the deeper follicles which lead to the acute reaction and a more speedy resorption, and thereby more quickly produce an allergic state. In this the passage of the fungi into the blood can also play a rôle. Through all these factors, the characteristics of the deep trichophytic diseases are produced; namely, deep inflammation, a quick destruction of the fungi, strong healing tendencies and but slight resistance to therapy.

The reaction in deep tricophytic diseases is "adequate" at least in the acute forms. In experimental infections of animals one can demonstrate histologically that the fungi are eliminated with the tissues and that autoinoculations are probably prevented by the allergy. By analogy, the destruction of the fungi also takes place in the kerion. The microbes, deprived of their natural domicile, usually cannot survive in the granulation tissue.

Moreover, tricophytids were first observed in deep trichophytic infections. The first of these was the so-called lichen trichophyticus, the different forms of which simulate the spinous seborrheic or papulovesicular eczema, or even scarlatina. To these forms there have been added those similar to erythema exudativum and nodosum. The trichophytids, as is known, are not only observed associated with deep trichophytosis, but also with superficial forms: with microsporia, favus and, above all, with a particularly interesting form in mycosis of the feet (as Dr. Williams has assumed and as it was lately proved in Bloch's clinic [Werner Jadassohn and Peck]). In the latter cases, the lesions on the hands, which are without demonstrable fungi, must in an analogous manner be considered as mykids (dermatophytids).

In this entire group, it is particularly clear how the peculiarities can be explained by immune biology. In a great majority of cases, trichophytids are undoubtedly caused by hematogenous infection of the skin. It must be left undecided whether the fungi arrive in the skin, which has already become allergic, and there cause the trichophytid, or whether they have been previously deposited in the skin and the reaction occurs only when the allergic state has reached a certain development. (The reaction can possibly be due to the deposited endotoxins; the lack of peripheral growth, the almost constant absence of fungi, the long duration, particularly of the spinulous forms [adhesion of endotoxin], are to be explained on this basis.) The predilection for follicular localization is to be explained by peculiarities in the distribution of the blood vessels to the follicles, just as in other hematogenous exanthems, but perhaps also through the so-called keratophilia of the fungi. Trichophytids can probably also be caused ectogenously, as is shown by their localization on the neck and face in some cases of kerion. In these cases, one can see all passages from superficial trichophytic lesions to tricophytids. Correspondingly, there is the production of lesions, particularly lichenoid lesions, in trichophytin reactions. In the rare corymbiform trichophyton infections there is probably transport through the lymphatics, or there is a stronger reaction in the vicinity of the lesion to those fungi which were brought there by the blood. Experiments on animals speak for the correctness of all these deductions, for according to variations of the conditions of the experiments on intracardial reinfection, all intermediate forms from normal reaction to immunity ensue, and in the middle of this scale there may appear types corresponding to trichophytids.

The relationship of immune biology to the morphology and course of the superficial trichophytic infections is much less clear than its relationship to the deeper forms. In the superficial forms, trichophytin reactions either are not present or are insignificant, except in those cases in

which long duration or the infection of a large area have led to an increased production of antibodies. In the smooth mycotic infections of the heads of children, the peculiarities, which consist of a lack of strong inflammatory symptoms, a persistence of large numbers of fungi and a lack of healing tendencies, are those which can be explained by the feeble development of the allergy. The latter cannot be due to the localization of the fungi, because they penetrate into the depths with the hairs, just as in the deep mycoses. The spontaneous healing which takes place at puberty without any acute signs of reaction cannot be connected with the allergy. In some of these mycoses one can more readily connect with the allergy the fact that the infection does not spread over the entire head, and that lesions which appear later remain smaller.

In the superficial forms of trichophyton infections of the glabrous skin the typical developments of form are those which have been regarded as characteristic for parasitic dermatoses, i. e., central healing, ring formation, the results of confluence, and recurrences in the centers. In spite of this, there has been but little advance in immune-biologic understanding of these manifestations. This may be due to the fact that experiments on animals and trichophytin tests could not bring clearness on these points. In this respect, the reinfection of trichophytic lesions with cultures of fungi has proved decidedly more useful to my collaborators (Epstein, Grünmandel) as well as to Martinotti in investigating other questions: These experiments showed that the reinoculation of skin sites which have been healed shortly before give a positive result. However, the infection almost always takes place only in the surrounding previously unaffected tissue (compare Greenbaum) and even leaves free a peripheral zone from 0.2 to 2 cm. in breadth around the most external points which had been previously affected. In this zone could be occasionally observed an early inflammatory reaction, but never the development of a tricophytic infection. The scratch, as used for illustration, showed a diminishing development, corresponding to the differences in reaction to trichophytin or fungi which Pedderson, Sutter and Kogoj [1] observed to take place according to the distance from the diseased skin area.

This immune zone was missing when the reinoculation took place on lesions which were still in a state of growth. This difference between the behavior of the skin in the immediate vicinity of already healed lesions and of lesions which are still growing seems to me of fundamental importance.

1. The experiments of Kogoj cannot be directly compared with ours, as he dealt with deep trichophytic infections in animals.

A peripheral or ring zone has also been observed in irradiated skin and in psoriasis (Kropatschek and Linser, Woronoff). It seems logical to connect this zone with the cessation of growth of the lesion and with spontaneous healing. In this it is possible that the fungi may die at the inner margin of the zone, or may enter but create no pathogenic action within the zone. This question is not yet decided, but certain experiences in syphilis make one think that the latter may be true. From certain experiments on animals, one can conclude that the fungi only multiply vigorously when they have caused a certain inflammatory reaction (Inga Saeves); such a reaction does not seem to take place in this refractory zone. It can now be understood why superficial trichophytic diseases heal spontaneously (though they do so in a variable length of time according to the person, kind of fungus and localization), in spite of the fact that the reaction to trichophytin seems to be lacking —for the latter is still to be considered a relatively crude method of testing.

Central recurrences can be explained thus: Fungi which have remained behind can once more become pathogenic when the immunity which was also present in the center has ceased to exist. The cocard forms can be explained by the peripheral growth of repeated central recurrences, or by the formation of several immune zones which are traversed by the growing fungi without causing a reaction.

The well known extinction of the points of contact of adjacent rings is caused by the fact that each growing ring reaches the immune zone of its neighbor. The forms of superficial trichophytic infection in which follicular papules containing fungi develop and persist for some time in the superficially healed areas are also interesting. These are seen not infrequently. They demonstrate how specifically localized the immunity may be, for in these cases there is sufficient immunity in the remaining epidermis and not enough in the follicular epithelium.

Of the other mycotic diseases I shall mention only the so-called herpetic form of favus as an example. In this form, the scutula show a predilection for central development. The skin remains anergic, and for this reason the fungi can for the moment develop in unhampered colonies, in contradistinction to what occurs in trichophytic lesions. Even in pityriasis versicolor the frequent circinary forms seem to prove the occurrence of immune biologic processes.

The second infectious disease which I shall discuss briefly is syphilis. I shall deal only with the questions of local immunity (which generally receive too little consideration), and will not discuss whether the spirochetes become changed through their sojourn in the body, or other questions of general immunity. The sometimes sudden development of the primary lesion, as well as its spontaneous healing in the period of

"immunity to primary lesion" which develops in the first stage, point to its origin as the result of an antigen-antibody reaction. The prodromal regional papules, as well as the circinary primary recurrences which are observed in animals, and which only grow toward the periphery, are to be attributed to a local immunity which has already developed in the region of the primary lesion. In the first roseolas, the majority of spirochetes are most certainly quickly destroyed. The roseolas develop either because through dying in the allergic skin the spirochetes cause foci of inflammation, or because the allergic reaction to the first dying spirochete itself kills the spirochete.

Leaving out of consideration the individual differences, both in the entire organism and in the skin, which affect the form of the lesions during the entire secondary stage, for instance, malignant syphilitic, seborrheic syphilis, etc., the following factors can be designated as determining the variability of development: the duration of the infection, the age and sex of the patient, the localization, the provocation and the sensitization. I will here mention only a few forms and the questions which arise in connection with them. The recurring annular or figured roseolas can be explained by the formation of a central region of immunity, regardless of whether these forms are attributed to spirochetes which have remained or to a new hematogenous distribution (the influence of the livedo reticularis, the nerves, etc., may perhaps also play a rôle). The papular recurrences correspond to a different state of allergy; here the reactions are more massive and more chronic. Their healing must be considered as due to local immunity, for while one lesion disappears, another may appear. (The free zones which occasionally appear about syphilitic papules in mercury dermatosis are analogous to such observations in trichophytic infections and in psoriasis.)

In case of circinary syphilitic papules, both the signs of local immunity and the analogies to trichophyton infections are particularly clear. The so-called corymbiform ("Bomben-Syphilide"—"bomb syphilids") have for a long time [2] been classic examples of such processes. That the satellite lesions stay behind the central one in their development is attributable to a partial regional immunity. Their frequent follicular localizations are due to the peculiarity of the follicular apparatus which I have already mentioned, and the cessation of the satellite lesions at the periphery is caused by the finally adequate local immunity and (of course, only temporary), complete immunity. Above all, however, the immune zone sometimes found between the central and the satellite lesions (according to Woronoff, this exists only clinically) represents an absolute analogy to the refractory zone demonstrable in mycotic infections. In these eruptions the occasional occurrence of several such groups in

2. Jadassohn, J.: Third Internat. Dermat. Congress, London, 1896, p. 352.

different parts of the body demonstrates that the state of general immunity is important for the development of these lesions also.

The great number of spirochetes found in condylomas is probably to be explained by the fact that local conditions favor their growth in spite of the existing allergy. Whether or not these lesions multiply through auto-inoculation is as yet undecided.

Lichenoid follicular syphilids demonstrate the importance of the follicles for hematogenous lesions, just as is the case in lichenoid trichophytids and tuberculids. In all these cases, the lack of peripheral growth is caused by the peculiarities in the conditions of immunity. The preference of the two last-named forms for children, and of this form of syphilis for the late secondary stage, points to the importance of the general condition of the organism in regard to these lesions. The not infrequent local positive Moro tuberculin reaction, which I was able to demonstrate in this type of syphilid, is particularly interesting as an immune biologic group reaction, at least for those who do not believe that this is a true double infection.

The oyster shell-like, crusted, rupioid syphilids are also of general interest. The crusts, which lie one above the other in layers, the oldest in the center, can only be explained by intermittent processes of exudation, by a certain rhythm which is frequently observed in pathologic events. This allergic process of elimination must alternate regularly with flare-ups of the disease. This reminds one strongly of the processes in the cocard type of trichophytic lesion.

According to our experience, secondary syphilis often shows a negative reaction to luetin. Naturally this does not disprove the importance of allergic phenomena; here also, like trichophytin the luetins are not capable of demonstrating finer and, above all, local differences. In tertiary syphilis of the skin the cutireaction is generally positive. It is interesting that with luetin I could not find differences in the allergy of the several zones in tertiary serpiginous syphilis, although Pasini could do so in tertiary lesions by employing spirochetes (compare trichophytic lesions). I cannot give in detail the distinguishing characteristics between secondary and tertiary periods. The most important is the "tertiary proportion between number of spirochetes and the type of pathologic process"; i. e., few spirochetes, and necrobiotic, often tuberculoid, granulations as tissue reaction. It is well known that in the various forms of tuberculosis, leprosy, leishmaniosis and blastomycosis, differences are found which are analogous to those in secondary and tertiary syphilis. While the gummas mainly originate in the subcutis and are more easily explained, the group of the cutaneous, the so-called tuberous, syphilids present a greater number of questions. The grouped nodules, the tertiary papules

of E. Lesser, remind one of the corymbiform processes, in so far as a region between the older and the newer lesions remains unaffected and therefore a dissemination takes place at the periphery. Not only is the previously affected region immune, but each lesion must have produced an immune zone also at its periphery. In the more confluent serpiginous and ulceroserpiginous forms, the arciform borders can in part be explained by the fusion of the rings, which come together in a manner similar to that in trichophyton lesions or in the secondary circinary arabesque-like syphilids. However, this does not explain the extinguishing of a greater or smaller part of the borders, which produces the well known kidney shape of the late syphilids. Besides mechanical conditions (tension and pressure), functional peculiarities of the skin must materially influence the local production of immune reactions, just as in fixed exanthems and refractory zones.

In serpiginous syphilids the peripheral growth ceases much later than in the circinary forms; in the former the immunizing influences at the margins are less effective, while the previously affected parts are permanently immune; the central remainders and recurrences are usually missing. In gummas also, spontaneous and complete healing is not infrequent, through elimination of the entire infected tissue or the destruction of spirochetes in the inflammatory wall. The association of tuberous syphilids with the gummas is relatively rare, perhaps through immunization of the skin by the subcutaneous processes.

The frequently observed fact that in the same patient either only gummas or only tuberous syphilids can be found points to individual differences in the various tissues or in the blood supply of the various regions. How specific the reaction of two tissues which are closely related embryologically (cutis and subcutis) may be is shown by the fact that the subcutis is much more prone to gummas, i. e., colliquation necrosis.

In malignant syphilis the strain of spirochetes or the reaction of the patient or both may determine the form—few spirochetes and a strong allergy to luetin are known to be typical here—and still the process is not identical with the tertiary one; rather, an as yet entirely inexplicable rôle must be played by individual conditions ("idiosyncrasy to spirochetes").

The same questions are to be considered in tuberculosis and in leprosy. The primary lesion of tuberculosis is best known through the inoculations at circumcision which take the form of an acute ulcerating process. In older children the primary complex of ulcer and regional lymphadenitis have even been observed; such ulcers can turn into a lupus.

In tuberculosis luposa or verrucosa one finds the common reaction of the cutis to tubercle bacilli. In this case there is usually an allergy, either caused by a preexisting internal tuberculosis which is present even though the tuberculoderm is attributable to external infection, or, probably much more rarely, caused by the tuberculoderm itself; in other words, the form of allergy determines the type of development of the infection. The importance of the specific reaction is also evident in tuberculosis ulcerosa, in the tubercular auto-inoculation in patients with severe tuberculosis, with their cachectic anergy, often showing an uncharacteristic histologic picture and large number of bacilli; it is also evident in acute disseminated miliary tuberculosis, which is the hematogenous analogon to the aforementioned condition. Lupus spreads in small lesions or serpiginously, like cutaneous tertiary syphilis. Corresponding to the more incomplete immunization, central healing is much less frequent than in syphilis. The rupioid serpiginous form of lupus is but little known. In this the development of the crusts in an intermediary zone between periphery and center corresponds to different forms of reaction in these parts. Like the gumma, tuberculosis colliquativa is particularly associated with the subcutaneous tissue. The occurrence of multiple subcutaneous and even cutaneous cold abscesses without the formation of lupus lesions shows that here also the individual disposition plays a great part.

Immune-biologic influences are of particular importance in the so-called tuberculids. In these also, the lack of tendency toward growth, the disposition to necroses, etc., are attributable to the allergic skin reaction. That one does not meet these tuberculids in cases of active pulmonary tuberculosis points in the same direction. An important rôle is played by lichenoid forms in children particularly and, as is well known, the nodular forms (erythema induratum) are frequent, particularly in young women. The phenomenon of local immunity is here also encountered (circinary lichenoid and nodular tuberculids). According to more recent investigations in my clinic (Martenstein and Noll), when one tests the reaction to tuberculin with graduated dilutions, one finds that on the average the sensitiveness is less strong in tuberculids than in classic tuberculosis of the skin. This fact seems to point to a sort of transition between tuberculosis through tuberculids to the so-called anergic group, particularly sarcoids and lupus pernio. Here the histologic and clinical picture in the skin, in the internal organs and in the bones, the presence of anticutines and procutines (Martenstein and Werner Jadassohn), and the occasional developing into hyperergic forms with the resulting change of picture all speak for this standpoint. Similar conditions seem to exist in lupus miliaris and in granuloma annulare. I

should still like to leave lupus erythematodes out of this discussion, for if this disease, or some forms of this disease, may belong to tuberculosis, other as yet absolutely unknown circumstances must here be at play. Here also not only the type of growth but also the acute eruptions point to immune-biologic phenomena.

I shall speak briefly of leprosy. Since my immune-biologic presentation of this disease (1913) this viewpoint has been continually gaining ground. While there is still too much ignorance concerning the primary lesion, one can assume without particular difficulty that the first hematogenous maculae develop into either one or the other of the two principal forms, according to the allergy formation in the person affected. Naturally, also, other factors can be of importance. The differences in the disease not only of the skin but also of the nerves can be explained by the variations of tissue reaction. The variations of allergy explain the tremendous differences in the number of bacilli found, the passage of the tuberous forms into the nervous ones, and the frequency of the mixed forms; they also explain the tuberculoid form, which I consider a form of transition. The acute forms, with necroses and bullae, met with in lepra lazarina and the acute reactions are best explained by this viewpoint.

A comparison of the three most important infectious diseases which localize on the skin shows that in all three there exist relationships between allergy, structure of the tissues and content of microbes which are of the utmost importance in the morphologic determination of the lesions. In these analogies, however, one must also beware of generalizations. Such a generalization lies, for instance, in the attempt to transfer the terms "secondary" and "tertiary" to lepra and tuberculosis. I shall only cite some differences between the otherwise similar papulonecrotic tuberculids with their lack of demonstrable bacilli, and the papular syphilids with their high content of spirochetes, or between the seemingly tertiary sarcoids with their anergy and the tertiary syphilids with their marked hyperergic reaction, etc. There are here still many riddles which are not to be solved by the drawing of analogies.

I shall not speak of leishmaniosis, blastomycosis, coccidioidal granuloma, etc., in the consideration of which entirely similar conclusions would be reached. I must also be brief in dealing with the acute infectious processes, of which there is still too little known in spite of a few recent investigations.

In pyodermas the great tendency toward spontaneous healing points to immune-biologic processes. In the individual lesions, the elimination of the infected tissue can play a great rôle. (Compare trichophytic infection in animals.) This is the case in furuncles as well as in impetigo, etc. In impetigo contagiosa the spontaneous healing, even

without therapy, can only be explained, it seems, by immunizing processes or by a weakening of the microbes. Impetigo circinosa, which is generally a staphylococcic disease, is to be considered analogous to trichophytia circinosa. A general cutaneous allergy can here play a rôle, even though it is not yet demonstrated, in spite of some new attempts in this direction. In erysipelas, sensitization and semi-immunity occur, and in erysipeloid, healing through immunization is certain.

More is known in the case of ulcus molle. This also heals spontaneously without the general demonstration of an allergy through the cutireaction. One must suppose here also inadequacy of the vaccine or local immunity. In cases with lympadenitis an allergy is demonstrable and in these there is an increased tendency toward the healing of the ulcer. The serpiginous ulcera mollia can now be explained by the lack of an immune marginal zone. In these, however, the general allergic condition may be altered (the occurrence of such ulcers with few bacilli in contradistinction to that which occurs in other individuals [Frei]).

In balanitis erosiva circinosa, often called the fourth venereal disease, one observes central healing, growth at the periphery, confluence of the lesions, a special disposition of the parts covered by the prepuce and spontaneous healing of the disease; in other words, phenomena which have long been well known in local infections of the skin.

In lymphogranuloma inguinale, the quick healing of the primary lesion and the cutireaction of Frei speak for the importance of cutaneous allergy. This, however, does not lead to a quick healing of the glandular alterations. In herpes simplex and zoster, immune-biologic discussions are the order of the day, but a solution is still far away.

I cannot here discuss other infectious dermatoses, but it seems important to point out that one must now think of immune-biologic processes also in toxicodermas. The central healing and peripheral growth which have been considered as characteristic of parasitic dermatoses are particularly to be found in the prototype of toxicodermas, in urticaria and its erythematous variations. Lewis, too, attributes the central healing and the extinction at the points of contact of two lesions to the fact that the blood vessels become refractory in the part first diseased. Even though the endocrine factor is assumed in dermatitis herpetiformis, this disease can be counted in the allergic group. Other examples of allergic reactions to toxins are found in the iris-shaped and cocard-shaped tuberculin reactions. If many idiosyncratic toxic dermatoses are attributable to antigen-antibody reactions (as is being more and more generally assumed), it is natural that these reactions should have a similar effect on the morphology of the lesions, as in infectious diseases. The morphologic differentiation between the ectogenous and endogenous

effects of the same substance is also apparent in toxicodermas (quantitative effect?). In the eczema which resembles trichophytic lesions, I should not like simply to assume the toxic viewpoint for the moment, as parasitic influences are here difficult to exclude.

These few words lead to those diseases of unknown etiology the morphology and certain other characteristics of which remind one of parasitic dermatoses. I shall mention only the most important. In psoriasis not only the well known circinary and serpiginous forms, but above all, also the rupioid and microrupioid, the microcircinary and the corymbiform lesions, just because they all occur here, remind one of parasitic rather than of toxic dermatoses. Woronoff found microscopically and macroscopically slightly differentiated zones about psoriasis lesions which have ceased to grow. This is in analogous to the observations in corymbiform syphilis. Woronoff believes that these zones in psoriasis show a changed reaction to various different irritations, in other words, a nonspecific resistance. The zones that resist inflammation and staining in treatment with chrysarobin may also be cited. The regular intermittence in the formation of the crusts in rupioid forms and in the microrupioid type is in contrast to the irregular distribution of the parakeratotic spots in the common form. The same contrast is found between the nail lesions of the microcircinary forms and those in common psoriasis of the nails. Thus, many points speak for the infectious nature of psoriasis. Even more than all the observations given, the experiments of Lennhoff point in this direction. These experiments with inoculation in psoriatic patients gave positive results only when psoriasis tissue was employed and cannot therefore be attributable to a simple provocation.

In psoriasis also, the morphologic similarities of lesions in the same person, and the differences according to the various sites of localization point to the importance of the individual type of reaction and of regional differences in the skin. In so-called seborrheic eczema, in parapsoriasis and particularly in lichen planus, one finds clinically very similar conditions (circinary, corymbiform lesions and acute dissemination from chronic lesions). The attempt to consider lichen planus as a reaction type, as the French authors and recently Buschke have, on the grounds of the existence of arsphenamine exanthems resembling lichen planus, does not seem to me to be justified. A long time ago, I pointed out the similarity in forms which exists not only between arsenic dermatoses, psoriasis and lichen planus, but also between dermatoses and conjunctivitis due to arsenic on the one hand, and those due to gonorrhea on the other. This last fact only gives a further example of the similarities of toxic exanthems with the aforementioned conditions, which are probably of an infectious nature, and therefore the probability of the infectious

nature of lichen planus cannot be refuted. Entirely the same considerations are in place in erythema exudativum multiforme (iris and circinate forms), and in erythema nodosum with its surely toxic doubles ("imitators"). I shall mention further only pityriasis rosea in which, particularly if a primary plaque is present, the incomplete development of the secondary elements and the tendency toward spontaneous healing speak for the infectious nature (entirely in accord with Wile's experiment). On the other hand, there is exfoliatio areata linguae, which surely looks "parasitic," but in which the exceptionally transient character of the lesions reminds one more of the urticaria which shows peripheral growth (urticaria centrifuge?). I further mention the etiologically unclear purpuras with ring formation (including purpura Majocchi). I mention also alopecia areata, vitiligo, erythema migrans, and the puzzling formations in mycosis fungoides.

From all these considerations, the following conclusion is to be reached: There are a number of etiologically unclear dermatoses the infectious nature of which is made very probable by deductions of analogy; the analogies between infectious and idiosyncratic toxic conditions, however, must now make one particularly careful.

In order to have included all the diseases in which the circinary or serpiginous form recalls parasitic lesions, I must also name the infrequent benign tumors, the infective angiomas of Hutchinson, the rare case of "syringoma circinosum" (Nägeli, published from my clinic in Berne), and the keratoses and other nevoid formations. In addition to the spontaneous scarlike healing of the oldest and most central parts, an apposition of single lesions in ring form might be considered. The latter has been considered also as a possibility in psoriasis, granuloma annulare, etc. Both of the possibilities described do not entail any connection of these tumor forms with immune-biology.

As is well known, the occurrence of central, and at least partial, healing processes, is much more frequent in basal cell epitheliomas than in benign forms. In malignant tumors the attempts at healing through the reactive processes in the surrounding tissue are sufficiently well known. In these, since Ehrlich's investigations, one can think also of immunizing phenomena, without being forced to postulate a parasitic etiology of cancer based on their peculiarities of form.

I myself know best how incomplete these remarks have been and how much of all this is necessarily hypothetic. Little is known as yet of the relationship of immune-biology to the morphology of dermatoses, but enough is known to attempt a systematic compilation. Such a compilation will best bring to light the gaps in the knowledge.

ABSTRACT OF DISCUSSION

DR. CHARLES MALLORY WILLIAMS, New York: I shall refer briefly to a case that brings up several points mentioned by Professor Jadassohn.

A man came to the Skin and Cancer Hospital with a ringworm infection of the left side of the face, including the upper lip, enlarged tender glands of the neck and a temperature of 101 F. Mycelia were found in the lesions from the hair in the chin and lip. Many cultures were made but they produced nothing but *Aspergillus,* which was probably a contamination. Blood cultures were negative. Repeated examinations and cultures afterward were always negative. The man remained sick, the swelling of the glands remained, and he improved only after he was given intravenous injections of a compound solution of iodine; then improvement was rapid. About two weeks after admission to the hospital, he developed a recrudescence on the right upper lip; again mycelia were found in the fresh lesions, and again later examinations were negative. Following this he developed a diffuse follicular trichophytide.

Why does kerion of the bearded face resist treatment, while kerion of the scalp is practically self-limited? Why was it that the patient's symptoms persisted long after it had become impossible to recover any organisms from the skin?

DR. FRED D. WEIDMAN, Philadelphia: One hesitates to discuss this most thoughtful address of Professor Jadassohn's, because justice cannot be done it in such a short time. It is the kind of address that appeals to the pathologically minded dermatologist. Professor Jadassohn has taken us on a pioneer tour through the skin, and after intimating the way in which reactions "normally" take place, he has demonstrated the factors that may be introduced from time to time to disturb the progression of these different forms. The phase that he stressed particularly was that of immunobiology, and, to repeat, it would be impossible for any one here to discuss such a subject adequately in the ten minutes allotted. Hence one can only recite personal experiences and impressions that one may have had in the field that Professor Jadassohn has been covering. For that reason our discussion must be most desultory.

I wish to call up, for one, the annular lesions that are seen in ringworm. By analogy, the botanist has known the "fairy rings" of forest glades for a long time, and it has been determined that this form is assumed because there is a subterranean fungous growth, like truffles, which affects the growth of flowers overhead. Thus, as the fungus dies out centrifugally (exhausts pabulum), it decomposes and becomes a fertilizer and there is an overlying growth of flowers in the form of a ring. That is not an immunobiologic mechanism, but just a matter of nutrition, which would be analogous to what Professor Jadassohn has cited, in dermatology, as a body state, which is not general, but local.

A matter of interest is that of local immunity as perhaps a eugenic phenomenon. I recall a case reported by Dr. Markley in which there was sensitization to guinea-pig hair; the patient was sensitive in some places on the body and not in others. Perhaps it is proper here to invoke the mosaic law of inheritance with which the geneticist is familiar.

All I can say further is that perhaps we are envious of Germany in having such an advocate of pathology in the advancement of dermatologic science.

DR. HAROLD N. COLE, Cleveland: As Dr. Weidman said, this paper is not the type that can be discussed well, but it is the type of work that has been carried on in Professor Jadassohn's clinic for many years, and it gives us all food for thought. If Professor Jadassohn never did anything else, his work on immune biology alone is of inestimable benefit to dermatology. When one thinks of the

work done, notably with tuberculosis of the skin, but also with other granulomas, with "oriental boil," with the fungus skin diseases, and so on, it is realized that practically every infectious line of diseases of the skin has been covered by him and his assistants. German medicine and medicine in general are greatly indebted to him for the valuable contribution that he has been making all these years.

DR. JAY FRANK SCHAMBERG, Philadelphia: We are greatly indebted to Professor Jadassohn for his beautiful and extremely concise presentation of his work on local immunity. We have been inclined, perhaps, to glance at the distribution of lesions on the skin without crediting to it its peculiar significance. The work of Professor Jadassohn and his associates is important because through careful study they are endeavoring to acquire facts which will be of benefit and will permit the formulation of definite laws. This requires many years.

I have thought for many years that acute infectious diseases and their outcome are largely the result of the virulence of the infecting organism. I believe it is true that smallpox, scarlet fever and other acute infectious diseases maintain commonly a definite type throughout an epidemic, whereas with chronic diseases, such as syphilis, tuberculosis and leprosy, to which Professor Jadassohn alluded, the important factor of reaction between parasite and host is a question of the resisting power or defensive mechanism of the patient. This no doubt influences local immunity as well as general immunity.

I am sure I echo the sentiment of all the members when I state that we have profited by this paper and are honored by its presentation.

DR. LLOYD W. KETRON, Baltimore: I am interested particularly in the question of immunity in one of the various diseases which Professor Jadassohn has discussed, namely, tuberculosis. It is generally recognized that the type of experimentally produced tuberculous infection in animals depends on the allergic state of the animal, and on the number of organisms injected. One can get an acute, intense reaction with a small number of organisms and a large amount of allergy, or with a large number of organisms and a low degree of allergy. On the contrary, a chronic, granulomatous type of cellular response occurs if either one or both of these factors is of a sufficiently low content or degree. In extensive tuberculosis of the skin in a patient recently treated, who presented a picture resembling a superficial lupus, both clinically and histologically, the patient was absolutely anergic to tuberculin, even in 10 mg. amounts, and there was no focal reaction to applications of tuberculin ointment. Rabbits, guinea-pigs and pigeons inoculated with tissue from the lesions did not develop tuberculosis. Such cases are difficult to understand, in view of experimental tuberculosis, when there is neither allergy nor apparently enough organisms to permit demonstration.

I should appreciate Professor Jadassohn's view of the matter.

PROFESSOR JADASSOHN: I thank you for the manner in which you have judged my feeble effort to speak about one of the most difficult questions, not only in dermatology, but also in general medicine. I wish to answer first the questions that were asked.

It is very difficult to give an explanation for the case that Dr. Williams mentioned. There must have been a strong allergy, judging by the clinical description given. One can imagine that even fungi which are still to be seen microscopically are damaged in such a manner that they do not grow in culture mediums. I have never seen such a case and can only try to give an explanation.

Concerning the resistance of kerion and sycosis to treatment, I only say that according to my experience in Berne and Breslau, the kerion-like forms of sycosis are perhaps somewhat more difficult to cure than most cases of kerion on the

heads of children, but are nevertheless much more easily cleared up than furunculoid types of mycotic sycosis. I frequently found the kerion type in Berne and the furunculoid in Breslau during the war. The latter was generally caused by *Tricophyton cerebriforme,* and was so rebellious that I was obliged to treat it with roentgen epilation. Both forms of sycosis may show a strong reaction to trychophytin; nevertheless the tendency toward healing may be different. The resistance in Dr. Williams' case can be explained by the fact that the fungi remained in the tissues, or that, as in lichen spinulosus trycophyticus, only endotoxins may have remained.

Concerning Dr. Weidman's remarks, local sensitizations play a great rôle in these questions. Many years ago I observed a case of local sensitization to "Odol," a mouth wash containing salol or a related substance. This case and others from my material, as well as facts from the literature, formed the basis for one of my last publications on this problem. The relations between local and generalized sensitization of the skin require further study.

I agree with Dr. Schamberg that a distinction must be made between the immunizations occurring in acute and chronic infections. There are also important differences between the different chronic diseases, as I pointed out in my paper concerning syphilis and tuberculosis. There also exist interesting analogies between infectious processes and those produced, for instance, by iodides. Many years ago (Toxicodermien, *Deutsche Klinik,* in 1903) I observed cases of iodism; the first attack came after a certain dose of iodide of potassium. After some time, the same dose was tolerated, or it produced the same symptoms of iodism; later, the patient could be immunized by slowly increased doses. In other cases the so-called erythema nodosum existed or developed several times after the same doses, or only after increased doses. One can thus compare the different forms of sensitization and desensitization in toxic and infectious diseases.

The interesting case mentioned by Dr. Ketron may be one of the anergic group of cases of tuberculosis of the skin. It is known that rare cases resembling lupus vulgaris can be anergic, and that cases exist which are histologically, clinically and in their reactions, transitional forms between the so-called classic forms of tuberculosis and the anergic forms.

I wish to express my thanks once more for the kind words of Dr. Cole and Dr. Weidman. Since the time I noticed the importance of the proportion of few microbes and strong tissue reactions in chronic tuberculosis and tertiary syphilis, in 1895, I always was much interested in this question. I am convinced that in general pathology and in dermatology the relations between numbers of microbes, allergy and tissue reaction are of the greatest interest, and must be studied in all infectious diseases.

MERCURIAL OINTMENTS IN THE TREATMENT OF SYPHILIS

THEIR ABSORPTION AS MEASURED BY STUDIES ON EXCRETION *

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Mercury has been used by the inunction route in the treatment of patients with syphilis almost since the first authentic reference to the disease. Mercurial ointments have been used in the treatment of persons with diseases of the skin since time immemorial; what then could have been more natural than that some investigator should have employed it experimentally when syphilis first appeared on the medical horizon? Thus one finds that among the earliest writings on syphilis the use of mercurial ointments is recommended. For example, among the ten incunabula on syphilis reviewed by Singer,[1] Schelling (1495), Grunpeck (1496), Torella (1497), Widman (1497) and Steber (1498) emphasize the value of this medication; though Leonicenus rather discredited its value. Naturally, these early writers had little rime or reason to their methods of therapy.

The Spanish syphilographer, Almenar, in 1501, seems to have been the first physician to employ a rational method in the use of inunctions. He treated the patient rather than the disease. It seemed to be the aim

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* The special ointments were for the most part obtained from Dr. Fullerton Cook, chairman of the Revision Committee of the "United States Pharmacopeia." Many of the specimens were prepared under the supervision of the Philadelphia College of Pharmacy and Science.

1. Singer, C.: The Earliest Printed Literature on Syphilis, Florence, R. Lier & Co., 1925.

of most of the early syphilologists to salivate as soon as possible and as much as possible. In fact, this idea continued to be followed almost until the nineteenth century when, as a result of warnings from various physicians, among others Mathias'[2] "On the Mercurial Disease," physicians seemed to be a little more careful in the use of this remedy.

It is true that up to this time mercury had been used in many other ways, but inunctions were still popular vehicles for the drug. Moreover, they have continued to be used to the present day, and we find that many good syphilologists still include them in their armamentarium. It was felt for a long time that the inunction was absorbed, not only from the skin, but also through the lungs, through volatilization from the warm skin. On this theory the mercurialized flannelet of Merget[3] and the mercury pouch of Welander[4] were suggested. However, the experiments of Wile and Elliott,[5] and of Schamberg, Kolmer, Raiziss and Gavron[6] gave strong evidence against inhalations as the essential mechanism of absorption. In a former paper,[7] we discussed the work of Neumann[8] and Fürbringer[9] who found that the mercury absorbed from the skin is taken up in the form of fine mercury globules rubbed into the hair follicles and possibly into the openings of the sweat ducts. Their observations have been confirmed by Zwick[10] in a microscopic study of the skin treated by inunction with mercury. These authors found that the absorption of the mercury from the follicles was probably influenced by sodium chloride, fatty acids and albuminates of the body. They questioned whether any mercury was absorbed from the surface of the intact skin. Only the mercury globules rubbed into the follicles were gradually absorbed. On the strength of this suggestion, we devised the clean inunction[11] method of administering mercury by the

2. Mathias, Andrew: On the Mercurial Disease, Philadelphia, Parker, 1810.

3. Merget: Mercure: Action Physiologique, toxique, et therapeutique, Bordeaux, Paris, 1894.

4. Welander, E.; Arch. f. Dermat. u. Syph. **25**:39, 1893; **40**:257, 1897; **46**:39, 1898; **54**:59, 1900; **82**:163, 1906.

5. Wile, Udo J., and Elliott, J. A.: Absorption of Mercury, J. A. M. A. **68**:1024 (April 7) 1917.

6. Schamberg, J. F.; Kolmer, John; Raiziss, G. W., and Gavron, J. L.: Absorption of Mercury, J. A. M. A. **70**:142 (Jan. 19) 1918.

7. Cole, H. N.; Gericki, A. J., and Sollmann, Torald: Clean Inunction Treatment of Syphilis with Mercury, Preliminary, J. A. M. A. **77**:2022 (Dec. 24) 1921.

8. Neumann, J.: Wien. med. Wchnschr. **21**:1209, 1871.

9. Fürbringer, P.: Arch. f. path. Anat. **82**:2491, 1880.

10. Zwick, Karl G.: Microscopic Study of Mercury Absorption from Skin, J. A. M. A. **83**:1821 (Dec. 6) 1924.

11. Cole, H. N.; Gammel, John; Rauschkolb, J. E.; Schreiber, Nora, and Sollmann, T.: Clinical Excretion of Mercury After Intramuscular Injections of Mercuric Bromide, After Simple and After Clear Inunction, Arch. Dermat. & Syph. **17**:625 (May) 1928.

skin. If the only mercury absorbed is that portion in the follicles, it is not necessary to leave the portion remaining on the outside, and it can be cleaned off after the rubbing, for example, by removing the excess with a cloth saturated with benzene. In practice we have found this to be more or less true, though it is probable that in the cleansing of the skin some of the mercury globules in the mouths of the follicles may be removed. From our studies on excretion, comparing the method of clean and simple inunctions, we were forced to conclude that variation in the excretion of different patients treated by the same method was much wider than the differences between the medians of excretion of the two methods.

The urinary, fecal and total excretion of mercury was studied in three groups of patients treated with intramuscular injections of mercuric sodium bromide (10 mg. per day), simple inunctions and inunctions with subsequent removal of excess ointment by benzene. In all, the rate of excretion increased with the duration of the administration, but at somewhat different rates. At the end of the usual three or four weeks' course, the total daily excretion averaged from 1 to 1.5 mg.; the extremes from 0.5 to 3.5 mg. With simple inunctions, it averaged about a fourth greater, and with clean inunctions about a fourth less, than with the injections. The ratio of mercury in the urine to that in the feces varied widely. The urinary excretion was relatively higher after intramuscular injections; the fecal excretion, after inunctions. This is probably due to the conveyance of some of the ointment from the hands of the patient to the mouth. The total amount of mercury excreted in the four weeks' course of injections averaged 21 mg., of which 15 mg. was in the urine. With simple inunctions, the total excretion was a fifth greater, and with clean inunctions, about a fifth less. After discontinuance of the administrations, the excretion continued to be high for a considerable time.

The volume of the urine had no constant effect on the urinary excretion of mercury; the fecal excretion tended to vary with the weight of the feces.

When the method of inunctions is used, men excrete more than women; this is attributable to more vigorous rubbing. Negroes excreted more than white patients, perhaps because of less thorough removal of ointment from the hands.

In most patients the salivation depends on the intensity and on the duration of the excretion of mercury, but patients hypersusceptible to stomatitis may develop this condition early, when the excretion level of mercury is still low.

We also found in this study that even if a patient's skin was not intact in his disease he did not necessarily absorb more mercury than with a normal skin. The patient with an extensive syphiloderm showed

no higher excretion than the ones with clear skin. Moreover our studies on salivation confirmed these observations, and we have recently been able once more to confirm them in our study of the use of massive inunctions given once a week. In this study, massive inunctions of the body with 30 Gm. of mild mercurial ointment, U. S. P. 30 per cent, equivalent to 9 Gm. of metallic mercury were made by two men rubbing for sixty minutes once a week for four weeks. The ointment was applied generally but especially to the chest, thighs and forearms. There was little or no irritation of the skin. Slight salivation was noted in but one of the six cases.

Studies on excretion showed a greater and more rapid cumulative excretion of mercury by the urine and as large an output by the feces as with the 50 per cent simple inunctions, the 50 per cent clean inunctions, the 25 per cent simple inunctions, and the daily injections of bin-bromide of mercury. The mercurial excretion in the after-period of

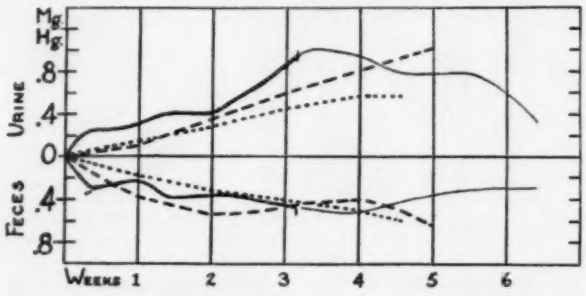

Chart 1.—Comparison of medians of weekly and daily inunctions. The heavy black line indicates the medians for massive weekly 30 per cent mercury inunctions; the light line, the after-period. The heavy dotted line indicates medians for daily simple 50 per cent mercury inunctions, and the fine dotted line indicates medians for clean 50 per cent mercury inunctions. The explanation of the symbols used in the succeeding charts is as follows: M, male; F, female; Wh, white; Bl, black; T, teeth; g, good; f, fair; p, poor; D, derma; O, no objective symptoms; mac, macular eruption; pap, papular eruption; squam, desquamating; exf, exfoliation; Sx, salivation. The arrow indicates that further inunctions were stopped.

four weeks was also similar to that following daily inunctions. It seems to us that this technic may be of value in those ambulant cases requiring weekly supervision of the condition.

However, there are some other factors to be considered in connection with inunction therapy which we might briefly mention before more thoroughly considering each in its order. Does the amount of mercury present in the preparation have any effect on the mercurial excretion and also on the antisyphiltic property of the ointment? In other words, would the effect be the same from the 25 per cent mercury ointment as from a 50 per cent or a 5 per cent preparation? To our knowledge

this question has never been scientifically decided. Again, does the character of the base have any influence on the absorption? There are several patent mercurial preparations on the market which are recommended for use simply by patting them on the skin. The manufacturers claim that due to the character of the base the mercury is absorbed at once. Is this true or is it rather the case that the base is quickly absorbed leaving the mercury still present? It is evident that the subject of different bases for mercury is a question which should be solved. Should we use a thin ointment or a stiff ointment? Or possibly should we use it in the form of an oleate? The question arises whether mercury in this form might not be absorbed even better from the skin. Wild and Roberts [12] from a rather crude method of scraping off mercury ointment with a dull razor blade from approximately 20 square inches of skin and weighing this excess found that there was 15.98 per cent average absorption of the 30 per cent British Pharmacopeia mercury in a lard base. In a soft paraffin base it was but 8 per cent, and with hydrous wool fat they found the base to be absorbed and the mercury left on

TABLE 1.—*Daily Excretion of Mercury, Fifty Per Cent Simple Inunctions of Mercurial Ointment*

	Total	Urine	Feces	Urine/Feces
First week.....	0.56 (0.18-1.02)	0.12 (0.02-0.4)	0.35 (0.02-0.72)	0.6 (0.1-4.7)
Second week.....	0.94 (0.52-1.45)	0.33 (0.15-0.7)	0.48 (0.30-1.25)	0.6 (0.1-2.3)
Fourth week.....	1.44 (0.78-3.52)	0.83 (0.38-3.0)	0.45 (0.18-2.0)	2.3 (0.7-11.6)
Sixth week.....	.....	0.98 (0.55-1.45)	0.72 (0.35-1.05)	1.2 (0.6-1.8)

the skin. It is true that their method was rather crude, but when one remembers that with each of these experiments the same technic was used, possibly we are justified in considering their data as more or less comparable. The question also arises as to whether the size of the mercury globule has any effect on the rapidity of the mercury absorption of the preparation from the follicle. According to the theory of Fürbringer and Neumann, one would expect greater absorption from a preparation with fine mercury globules, or even better in a colloidal form, than from an ointment with large mercury globules. How does this actually work out in practice? These and other problems will be discussed more thoroughly subsequently.

COMPARISON OF MERCURY OINTMENTS OF DIFFERENT PERCENTAGES

In a previous study, the medians of the milligrams of mercury excreted per day in a group of eleven cases in which 50 per cent simple inunctions were used were determined and are given in table 1.

For comparison with this, observations were made on a group of three men and four women, three of them being white and four colored.

12. Wild, R. B., and Roberts, Ivy, Brit. M. J. **1**:1076, 1926.

In six the teeth were good and in one fair. Three of the patients had no eruptions on the skin, three had papular syphiloderms, and one had a desquamation. They were treated with a mild mercurial ointment containing 25 per cent mercury. It was made up after the manner of the United States Pharmacopeia by diluting the stronger mercurial ointment, U. S. P., with equal parts of petrolatum and suet.

Four grams of this ointment was rubbed into the skin by the patient for thirty minutes daily for thirty-two days, making a total of 7 Gm. of mercury per week. The regions of the body were used in rotation in the usual manner. Specimens of excreta were collected as shown on the charts.

RESULTS

The daily excretion of mercury is shown in table 2. The data of the patients were plotted separately and combined and reduced to medians and extremes. The median urinary excretion curve shows a gradual progressive increase to the end of the fourth week, and then remains

TABLE 2.—*Daily Excretion of Mercury, Twenty-Five Per Cent Simple Mercurial Ointment*

	Total	Urine	Feces	Urine/Feces
End of 1st week...	0.37 (0.007-1.01)	0.12 (0.036-0.471)	0.15 (0.04-0.54)	0.87 (0.13-7.4)
End of 2d week....	0.45 (0.13 -1.77)	0.275 (0.06 -1.10)	0.265 (0.07-0.67)	1.64 (0.55-2.5)
30, 31, 32 days.....	1.09 (0.21 -1.94)	0.46 (0.08 -1.47)	0.43 (0.12-0.74)	1.73 (0.48-5.0)

about constant to the end of the course of treatment (thirty-two rubs). The median fecal excretion curve also shows a gradual regular increase to the middle of the fifth week, when the treatment was discontinued. The median total excretion curve shows a gradual increase to the middle of the third week and then remains fairly constant.

At the end of the fourth week the total mercury for 25 per cent simple inunction is about nine-tenths that of injection of binbromide; three-fourths that of simple 50 per cent inunction; four-fifths that of simple intensive inunction and four-thirds that of clean 50 per cent inunction. The urinary mercury for 25 per cent simple inunction is about one-half that of injection of binbromide; three-fifths that of simple 50 per cent inunction; one-half that of simple intensive inunction; and four-thirds that of clean 50 per cent inunction. The fecal mercury for 25 per cent simple inunction is about seven-fifths that of injection of binbromide; equal to that of simple 50 per cent inunction; nine-tenths that of simple intensive inunction and nine-tenths that of clean 50 per cent inunction.

The urinary-fecal ratio shows a gradual increase and is about the same as that of simple intensive inunction.

The median cumulative excretion is given in table 3. The total cumulative excretion is more like clean 50 per cent inunction; it is less than injection or 50 per cent simple inunction. In fact, the excretion is considerably lower than that of 50 per cent simple and about equal to that of 50 per cent clean mercury inunctions. The urinary excretion lies between simple and clean 50 per cent and is less than that when injections of binbromide mercury are given. In fact the urinary excre-

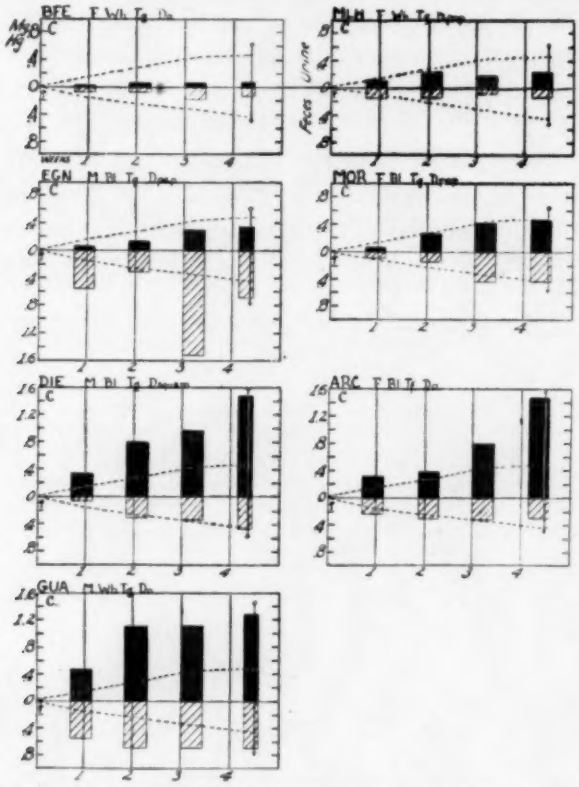

Chart 2.—Curves when daily simple 25 per cent (U. S. P. base) inunctions were used.

tion is about half that of 50 per cent ointment, i. e., practically proportional to the mercury content.

FIVE PER CENT SIMPLE MERCURY INUNCTIONS

Table 4 and chart 3 furnish the figures when a 5 per cent mercury ointment, U. S. P., was used. As can be seen, the contrast here is even more marked. The medians are slightly at variance as to days, but not enough to make any appreciable difference. In this series seven men were employed. All were white. Four of the patients had good

teeth, two fair teeth and one had poor teeth. There was one patient with varicose veins of the legs, one patient with a dermatitis of the hands and face and five patients showed no skin lesions. Salivation did not enter the picture in any of these cases.

TABLE 3.—*Cumulative Excretion (Median), Twenty-Five Per Cent Simple Mercurial Ointment*

	Total	Urinary
End of 1st week	1.11	0.50
End of 2d week	4.05	1.95
End of 3d week	8.58	4.38
End of 4th week	14.28	7.50
End of 32d day	17.81	9.34

TABLE 4.—*Simple Five Per Cent U. S. P.*

	Urine	Feces	Total	Urine/Feces
3, 4 days	0.02 (0.016-0.056)	0.10 (0.04-0.27)	0.12 (0.06 -0.31)	0.2 (0.14-0.93)
7, 8, 9 days	0.047 (0.03 -0.075)	0.16 (0.05-0.30)	0.22 (0.085-0.33)	0.46 (0.10-4.0)
14, 15, 16 days	0.07 (0.06 -0.16)	0.17 (0.06-0.34)	0.31 (0.122-0.44)	0.62 (0.21-1.1)
21, 22, 23 days	0.108 (0.06 -0.15)	0.28 (0.05-0.39)	0.39 (0.18 -0.49)	0.36 (0.17-2.7)
28, 29, 30 days	0.146 (0.12 -0.197)	0.25 (0.32-0.42)	0.38 (0.32 -0.59)	0.50 (0.35-1.4)
5, 6, 7 days after	0.089 (0.04 -0.14)	0.17 (0.07-0.36)	0.27 (0.11 -0.49)	0.37 (0.20-0.69)

TABLE 5.—*Comparison Different Ointments: Urinary Mercury Excreted*

	50% Simple	25% Simple	5% Simple
1st week	0.12 (0.02-0.4)	0.124 (0.036-0.471)	0.047 (0.03-0.075)
2d week	0.33 (0.15-0.7)	0.275 (0.061-1.102)	0.07 (0.06-0.16)
3d week	.....	0.43 (0.06 -1.11)	0.108 (0.06-0.15)
4th week	0.83 (0.38-3.0)	0.46 (0.08 -1.47)	0.146 (0.12-0.197)

TABLE 6.—*Comparison Different Ointments: Fecal Mercury Excreted*

	50% Simple	25% Simple	5% Simple
1st week	0.35 (0.02-0.72)	0.15 (0.04 -0.54)	0.16 (0.05-0.30)
2d week	0.48 (0.30-1.25)	0.265 (0.07 -0.67)	0.17 (0.06-0.34)
3d week	.....	0.33 (0.08 -1.52)	0.28 (0.05-0.39)
4th week	0.45 (0.18-2.0)	0.43 (0.123-0.74)	0.25 (0.32-0.42)

TABLE 7.—*Comparison Different Ointments: Total Mercury Excreted*

	50% Simple	25% Simple	5% Simple
1st week	0.56 (0.18-1.02)	0.389 (0.097-1.01)	0.22 (0.085-0.33)
2d week	0.94 (0.52-1.45)	0.449 (0.13 -1.77)	0.31 (0.122-0.44)
3d week	.....	1.10 (0.243-1.83)	0.39 (0.18 -0.49)
4th week	1.44 (0.78-3.52)	1.09 (0.21 -1.93)	0.38 (0.32 -0.59)

One notes a striking difference in the fall of excretion when the 5 per cent U. S. P. preparation is used as compared to the 25 per cent, or even more so if compared with the 50 per cent mercurial ointment. But to make our comparison even more striking it would be better to tabulate the medians of the urinary, fecal and total mercury excreted using the different methods in tables 5, 6 and 7.

In order better to compare this, we are presenting a chart (chart 4) showing the total mercury excreted, using the 50 per cent, the 25 per cent and the 5 per cent preparation. We are also presenting a chart (chart 5) giving a comparison of the cumulative excretion of mercury after simple 25 per cent, 50 per cent and 5 per cent daily inunctions (U. S. P. vehicle). We believe that these curves and the foregoing figures graphically show that the quantity of mercury absorbed from an ointment and excreted increases with its concentration and almost in direct ratio to the concentration of the metal.

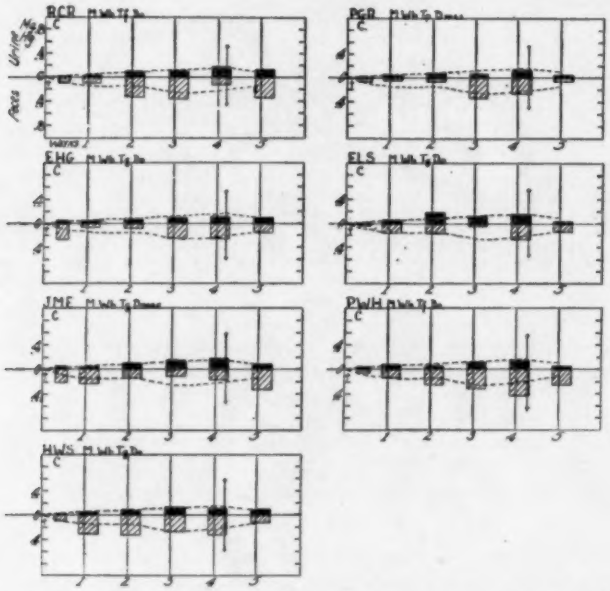

Chart 3.—Curves when daily simple 5 per cent (U. S. P. base) inunctions were used.

FUNCTION OF OLEATE IN THE ABSORPTION OF MERCURY OINTMENT

We have known for a long time that a part of the mercury in an ointment is gradually converted into an oleate, or soap, through the contact of the metal with the fat in the base. Binz,[13] in 1897, called this to our attention. Menschel [14] brought up this point again, mentioning the fact that the mercury probably not only is ionized in the oil ducts of the skin but also may be more or less converted into a soap while still in the ointment receptacles. He quoted Oberlin as having

13. Binz, C.: Lectures on Pharmacology, New Sydenham Soc. London, Adlard & Son, 1897, p. 132.

14. Menschel, H.: Biochem. Ztschr. **137**:193, 1923.

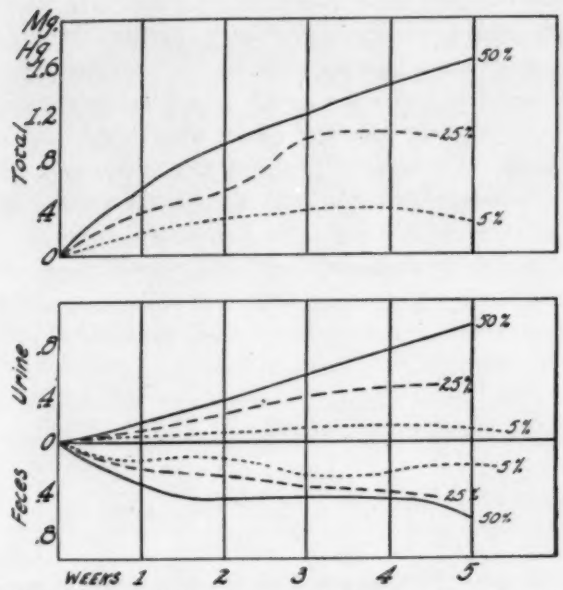

Chart 4.—Comparison of medians of daily excretion of mercury after simple 50 per cent, 25 per cent and 5 per cent daily inunctions (U. S. P. vehicle).

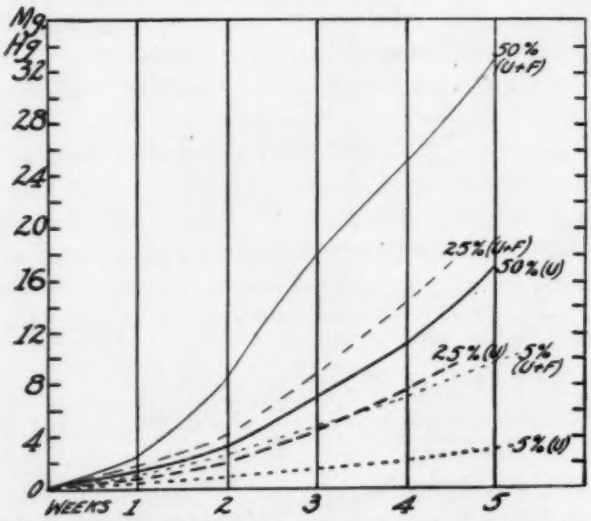

Chart 5.—Comparison of cumulative excretion of mercury after simple 50 per cent, 25 per cent and 5 per cent daily inunctions (U. S. P. vehicle).

examined sixteen year old preparations of mercurial ointment in which almost all the mercury was transformed into a soap. He found that in a fresh ointment from a Göttingen pharmacy that there was only from 0 to 0.01 per cent mercury oleate, while in one two months old there was already 0.15 per cent mercury oleate. In a machine made ointment, age unknown, 0.70 per cent mercury oleate was found, and in one at least three years old there was 4.7 per cent mercury oleate. He questioned whether this soap formation does not have a great influence on the absorption and therapeutic action of a mercury ointment. He also brought up the point that replacing lard with wax and paraffin would greatly lessen this oleate formation. Wild and Roberts concluded from their rather rough experiment that mercury was probably absorbed more rapidly from the oleate than from the metallic mercury ointment of equal strength. Thus, here again there are points which it is necessary to clear up in the problem of the absorption of mercury ointment from the skin.

TABLE 8.—*Results from Five Per Cent Oleate Soft*

	Urine	Feces	Total	Urine/Feces
3, 4 days.....	0.03 (0.02-0.06)	0.045 (0.005-0.335)	0.06 (0.027-0.37)	1.0 (0.11-3.0)
7, 8, 9 days.....	0.085 (0.04-0.14)	0.075 (0.035-0.41)	0.14 (0.102-0.495)	0.57 (0.21-2.6)
14, 15, 16 days.....	0.104 (0.07-0.14)	0.063 (0.051-0.45)	0.18 (0.13 -0.58)	1.65 (0.29-2.5)
21, 22, 23 days.....	0.139 (0.07-0.17)	0.147 (0.07 -0.18)	0.305 (0.22 -0.47)	1.0 (0.38-2.1)
28, 29, 30 days.....	0.143 (0.12-0.21)	0.151 (0.046-0.31)	0.298 (0.23 -0.51)	1.03 (0.53-3.9)
5, 6, 7 days after..	0.064 (0.06-0.096)	0.12 (0.02 -0.20)	0.19 (0.04 -0.24)	0.70 (0.18-1.5)

For this and for other reasons, it appeared desirable to test the absorbability of mercury oleate. Two ointments were made up, containing 4.8 per cent of mercury in the form of the oleate (i. e., 20 per cent of the U. S. P. oleate); one in benzoinated lard, which turned out to be rather soft; the second was made harder, of the consistency of the official ointment, by adding some suet and wax to the base.

Thirty rubs of the softer ointment were given to ten patients; and of the harder ointment to five patients. The results were practically identical in both series, furnishing, incidentally, an illustration that the routine of method of sampling and the number of patients are adequate. The results when the 5 per cent soft oleate was used are given in table 8 and chart 6.

The results of present significance are as follows:

1. The excretion increases progressively similar to that when the simple mercurial ointment is used. In the after-period it seems to decline more rapidly, indicating that less of absorbable mercury has accumulated unabsorbed in the skin. This contrast with metallic mercury might mean that the absorption of the oleate occurs at least partly through the epithelium, rather than from the ducts. However, it is only

suggestive and should not be emphasized until there is more direct evidence.

2. The level of excretion is considerably lower than with 50 per cent and even with the 25 per cent metallic ointment (simple inunction). The level of the daily urinary excretion at the end of the fourth week is shown in table 9.

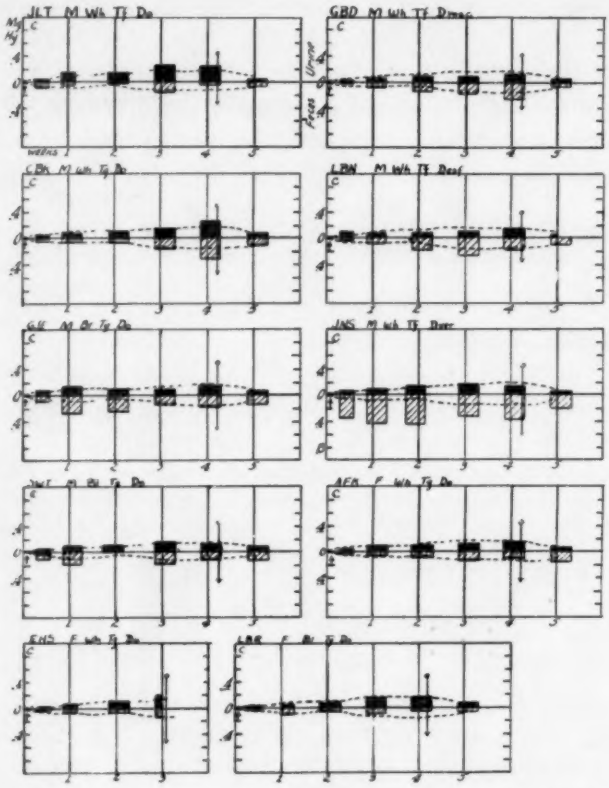

Chart 6.—Curves when daily simple 5 per cent oleate (soft) inunctions were used.

From the clinical standpoint, it may be remarked that the quantity of mercury absorbed from the oleate is probably below the level that is required for therapeutic efficiency in syphilis; and in agreement with this, not one of the patients showed salivation.

COLLOIDAL MERCURY OINTMENT

Some time ago, Squibb's Research Laboratory developed a process for making mercurial ointment which would provide the metallic mercury in a more or less colloidal state, and succeeded in producing an

ointment having a mercury content of about 50 per cent in wool fat. The maximum particle size was reported to be 8 microns and the average visible particle size 1.33 microns.[15]

The preparation was tried on six men, two white and four black. The condition of the teeth was good in four, fair in one and poor in one. In all six the skin was normal.

Studies made on the excretion of these six patients, with specimens taken at the respective days, showed the data as noted in table 10 and chart 7.

It was felt that through the use of a colloidal preparation of mercury that possibly the mercury would more easily penetrate the hair follicles and oil ducts, and being in the colloidal state would be more easily absorbed into the system. We would not have been surprised, consid-

TABLE 9.—*Daily Urinary Excretion at End of Fourth Week*

	Excretion Level	
	Mg.	Ratio to Oleate
Average of hard and soft oleate	0.17	1.0
50% metallic	0.83	4.9
25% metallic	0.48	2.8
5% metallic	0.146	0.86

TABLE 10.—*Results from Colloidal Mercury Ointment Fifty Per Cent*

	Urine	Feces	Total	Urine/Feces
3, 4 days	0.107 (0.05 -0.20)	0.09 (0.04-0.20)	0.22 (0.10 -0.35)	1.4 (0.47-3.0)
7, 8, 9 days	0.19 (0.098-0.30)	0.185 (0.13-0.52)	0.35 (0.187-0.77)	0.6 (0.4 -1.5)
14, 15, 16 days	0.31 (0.15 -0.32)	0.32 (0.16-0.39)	0.63 (0.31 -0.71)	0.87 (0.80-1.2)
21, 22, 23 days	0.72 (0.43 -1.77)	0.18 (0.15-0.24)	0.90 (0.58 -2.01)	4.0 (2.9 -7.4)
28, 29 30 days	0.96 (0.66 -1.97)	0.35 (0.17-0.60)	1.33 (1.26 -2.14)	2.8 (1.1 -11.6)
5, 6, 7 days after	0.78 (0.43 -1.13)	0.20 (0.10-0.31)	0.99 (0.75 -1.23)	6.3 (1.4 -11.3)

ering the theory of Neumann and Fürbringer, to find a higher excretion of mercury. Apparently, however, the absorption is no better with this type of colloidal mercury than with the ordinary 50 per cent mercurial ointment.

At the end of the fourth week the total mercury for 50 per cent colloidal mercury ointment is about equal to that of injection of binbromide; nine-tenths that of simple 50 per cent inunction; nine-tenths that of simple intensive injection and eight-fifths that of clean 50 per cent inunction. The urinary mercury for 50 per cent colloidal mercury ointment is about equal to that of injection of binbromide; six-fifths that of simple 50 per cent inunction; equal to that of simple intensive inunction and fourteen-fifths that of clean 50 per cent inunction. The fecal mercury for 50 per cent colloidal mercury ointment is about equal to that of injection of binbromide; four-fifths that of simple 50 per

15. The Squibb Laboratories furnished a supply of this ointment.

cent inunction; seven-tenths that of simple intensive injection and seven-tenths that of clean 50 per cent inunction.

The cumulative excretion median for the six patients under treatment with the colloidal 50 per cent mercury shows a median excretion as is shown in table 11.

As we study the curve of the total mercury in the colloidal form 50 per cent, with the 50 per cent simple and the 50 per cent clean inunctions we note some contrasts, though these are not especially marked.

What especially attracted our attention in connection with this ointment was the phenomenon in regard to salivation. Of the six patients

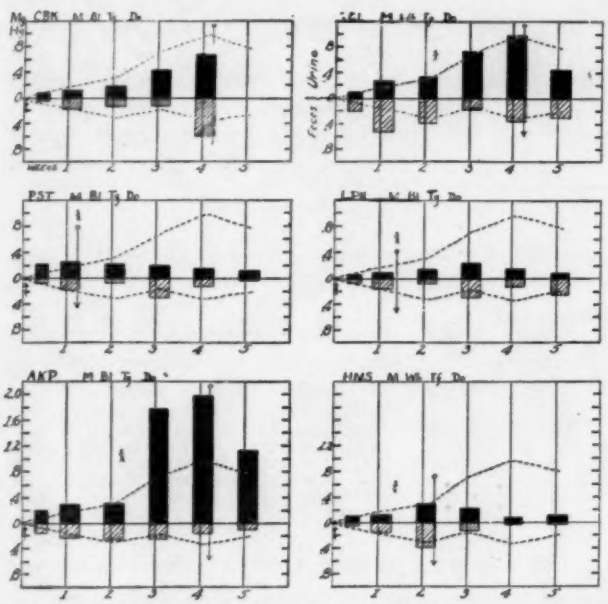

Chart 7.—Curves when daily simple 50 per cent colloidal mercury inunctions were used.

used, four had good teeth, one fair and one poor. Salivation was noted in all four patients having the good teeth, and also in the patient with poor teeth and there was gingivitis in one patient with good teeth. The salivation came on in series of eight, nine, ten, twelve and sixteen days with extremes of eight days and sixteen days and means of ten days. Gingivitis was noted in the other patient in twelve days. Salivation was so profuse in two of the patients, both of them with good teeth, that it was necessary to stop further use of the mercury in nine and ten days, respectively. It is difficult to understand these phenomena in contrast to our data on salivation in connection with other forms of mercury inunctions. As our charts and figures show, there was practically no

greater excretion with this colloidal mercury than with the other mercurial ointments; yet salivations are much more common. We do feel that this further confirms our previous statement that early salivation is necessarily connected with high excretion of mercury. In the hope of further elucidating this problem of absorption, solution, and excretion in connection with colloidal preparations six other patients were selected on whom a 25 per cent preparation of the same type of mercury was employed. Four of the patients were men and two were women; three were white and three black; the teeth were good in four cases and fair in the other two. One patient had a papular eruption but the others were normal. This was a case of extensive papulopustular syphiloderm. As can be seen from table 12 and chart 8 there was a surprisingly low excretion of mercury from these patients. This requires

TABLE 11.—*Median Excretion in Patients Treated with Colloidal 50 Per Cent Mercury*

	Total Mercury	Urinary Mercury
First week	1.5	0.82
Second week	5.1	2.6
Third week	10.5	6.1
Fourth week	18.2	11.9
Fifth week	26.2	18.0

TABLE 12.—*Results from Colloidal Mercury Ointment Twenty-Five Per Cent*

	Urine	Feces	Total
3, 4 days	0.175 (0 -0.025)	0.018 (0 -0.065)	0.039 (0 -0.083)
7, 8, 9 days	0.033 (0.013-0.056)	0.03 (0.02-0.20)	0.061 (0.053-0.22)
14, 15, 16 days	0.08 (0.029-0.23)	0.105 (0.04-0.16)	0.175 (0.007-0.37)
21, 22, 23 days	0.11 (0.04 -0.15)	0.075 (0.04-0.11)	0.193 (0.085-0.93)
28, 29, 30 days	0.14 (0.049-1.86)	0.105 (0.05-0.26)	0.34 (0.11 -1.95)
35, 36, 37 days	0.073 (0.024-0.77)	0.085 (0.02-0.24)	0.158 (0.047-1.0)

confirmation and it is planned to repeat the series. Moreover there was but one case of salivation in the group. This was noted in the patient with the papulopustular eruption, but being mild and not appearing until the twenty-fourth rub, the inunctions were continued until the full thirty were given. Moreover this patient's excretion of mercury from the urine at the end of four weeks was 1.86 mg. and from the feces 0.09 mg. in contrast to a median of 0.095 urinary and 0.12 fecal in the other five patients. This was contrary to our experience with absorption and excretion of mercury in other cases with skin eruptions. We quote it for what it is worth—perhaps the colloidal state may have something to do with it.

At the end of the fourth week the urinary mercury for 25 per cent colloidal mercury is about equal to 5 per cent U. S. P. base, ointment; one-third that of 25 per cent U. S. P. base, ointment and one-seventh that of 50 per cent colloidal ointment. The fecal mercury for 25 per cent

colloidal mercury is about one-half that of 5 per cent U. S. P. base, ointment; one-fourth that of 25 per cent U. S. P. base, ointment and one-third that of 50 per cent colloidal ointment. The total mercury for 25 per cent colloidal mercury is about equal to that of 5 per cent U. S. P. base, ointment; one-third that of 25 per cent U. S. P. base, ointment and one-fourth that of 50 per cent colloidal ointment.

The cumulative excretion at the end of the fourth week is as follows: The total mercury excretion is about one-half that of 5 per cent U. S. P. base, ointment; one-fourth that of 25 per cent U. S. P. base, ointment and one-fifth that of 50 per cent colloidal ointment. The urinary mercury excretion is about equal to that of 5 per cent U. S. P. base, ointment;

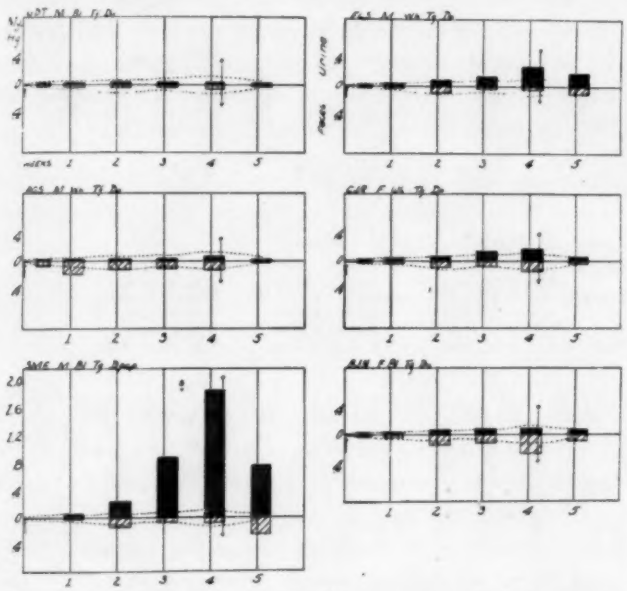

Chart 8.—Curves when daily simple 25 per cent colloidal mercury inunctions were used.

one-fourth that of 25 per cent U. S. P. base, ointment and one-sixth that of 50 per cent colloidal, ointment. The fecal mercury excretion is about one-third that of 5 per cent U. S. P. base, ointment; one-fourth that of 25 per cent U. S. P. base, ointment and one-fourth that of 50 per cent colloidal, ointment.

FURTHER INFLUENCE OF BASE ON ABSORPTION OF 50 PER CENT SIMPLE MERCURY OINTMENT IN PETROXOLIN

In order to study further the influence of bases on absorption of mercury from the skin we employed another preparation of 50 per cent mercury put up in the petroxolin of the "National Formulary." This base consists of white wax, 35; light liquid petrolatum, 20; oleic acid.

32; oil of lavender, 3; alcohol, 5 and stronger ammonia water, 5. In other words, the preparation consists largely of a soft soap. The mercury is mixed up with this base in the following amounts: mercury, 75; mercury oleate, 3 and solid petroxolin, 72, making a total of 150 Gm.

The ointment was employed on six patients, collections being taken as shown on chart 9. There were six men, five white and one black. The teeth in all the patients were in good condition, and their skins were normal. The excretion, as will be noted in table 13, is similar to that with the 50 per cent mercurial ointment. The base, apparently, has no particular influence on the absorption of the mercury.

A comparison of the 50 per cent petroxolin ointment with the other methods of administering mercury showed the following: At the end of the fourth week the total mercury for 50 per cent petroxolin is about eleven-tenths of simple 50 per cent inunction; twice that of clean 50 per cent inunction; eight-sevenths that of colloidal 50 per cent ointment; six-fifths that of injection of binbromide; seven-fifths that of simple

TABLE 13.—*Fifty Per Cent Simple Mercurial Ointment in Petroxolin*

	Urine	Feces	Total	Urine/Feces
3, 4 days.....	0.06 (0.02 -0.31)	0.05 (0 -0.33)	0.13 (0.02 -0.38)	0.23 (0 -2.1)
7, 8, 9 days.....	0.21 (0.06 -0.34)	0.12 (0.06-0.31)	0.31 (0.12 -0.63)	1.0 (0.51-3.7)
14, 15, 16 days.....	0.38 (0.10 -1.4)	0.37 (0.16-0.41)	0.78 (0.26 -1.77)	0.95 (0.63-3.8)
21, 22, 23 days.....	0.71 (0.145-1.5)	0.33 (0.23-0.69)	1.19 (0.415-1.84)	1.5 (0.54-6.5)
28, 29, 30 days.....	0.90 (0.175-1.58)	0.41 (0.07-0.84)	1.53 (0.455-2.42)	1.9 (0.7 -21.0)
5, 6, 7 days after..	0.57 (0.12 -0.80)	0.29 (0.10-0.84)	0.81 (0.21 -1.60)	1.1 (0.53-6.2)

25 per cent inunction and eleven-tenths that of simple intensive injection. The urinary mercury for 50 per cent petroxolin is about eleven-tenths that of simple 50 per cent inunction; thirteen-fifths that of clean 50 per cent inunction; nine-tenths that of colloidal 50 per cent ointment; nine-tenths that of injection of binbromide; twice that of simple 25 per cent inunction and equal to that of simple intensive injection. The fecal mercury for 50 per cent petroxolin is about nine-tenths that of simple 50 per cent inunction; four-fifths that of clean 50 per cent inunction; six-fifths that of colloidal 50 per cent ointment; four-thirds that of injection of binbromide; equal to that of simple 25 per cent inunction and four-fifths that of simple intensive injection.

At the end of the fourth week the cumulative mercury excretion was as follows: The total excretion for 50 per cent petroxolin is about equal to that following injection of binbromide; four-fifths that of simple 50 per cent inunction; six-fifths that of clean 50 per cent inunction; equal to that of colloidal 50 per cent ointment; thirteen-tenths that of simple 25 per cent inunction and three-fourths that of simple intensive injection. The urinary excretion for 50 per cent petroxolin is about eleven-tenths that of simple 50 per cent inunction; twice that of clean

50 per cent inunction; equal to that of colloidal 50 per cent ointment; six-sevenths that of injection of binbromide; eight-fifths that of simple 25 per cent inunction and three-fourths that of simple intensive injection. The fecal excretion for 50 per cent petroxolin is about one-half that of simple 50 per cent inunction; seven-tenths that of clean 50 per cent inunction; seven-sixths that of colloidal 50 per cent ointment; seven-sixths that of injection of binbromide; equal to that of simple 25 per cent inunction and seven-tenths that of simple intensive injection.

Studies on the salivation show that four of the six patients having good teeth showed salivation, in periods of six, thirteen, thirteen and thirteen days, respectively. There was gingivitis in one at nine days,

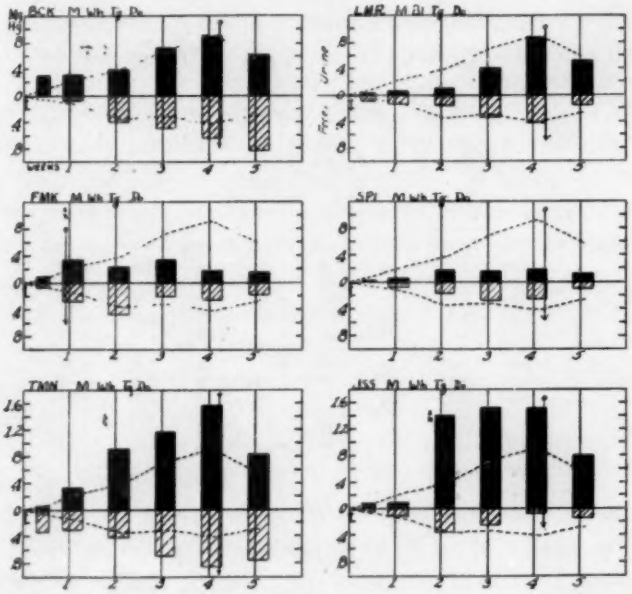

Chart 9.—Curves when daily simple 50 per cent (petroxolin base) inunctions were used.

and no salivation in one patient. It was necessary to stop the mercury because of salivation in but one patient, and that on the sixth day. This was probably a case of idiosyncrasy.

COMMENT

For several years we have been working on the phenomena of the absorption of mercury from the skin after inunction, as measured by excretion. There were several problems to be considered and solved if possible. Among others was the contention of Binz and Fürbringer that the only mercury absorbed was that retained in the follicles, notably the hair follicles. We suggested the clean mercury inunctions, based

on this theory, removing any excess ointment after the thirty minutes rubbing. Our studies on excretion have shown that the difference in the excretion by this method and that of the simple inunction was not so great as the variabilities found among patients using any other method. Zwick's microscopic studies of skin treated by inunction with mercury also tend to support and confirm the theory of Binz and Fürbringer and our contentions.

The present paper, we believe, proves without question that the absorption and excretion of mercury is dependent first of all on the concentration of the metal in the base used. In order to visualize this better, we are presenting in table 14 the data on the cumulative excretion for the varieties of mercury inunctions thus far studied.

Clinically in using mercury inunction in the treatment of syphilis the required mercury absorption and antisyphilitic effect will be lost if the

TABLE 14.—*Cumulative Excretion of Different Mercury Inunctions (In Descending Order of Mercury Excretion at End of Fourth Week, for Comparison)*

	End of First Week		End of Second Week		End of Third Week		End of Fourth Week		End of Fifth Week	
	Urine	Feces	Urine	Feces	Urine	Feces	Urine	Feces	Urine	Feces
30% intensive	1.74	1.89	4.54	4.36	9.34	7.16	16.00	10.40	21.72	13.14
50% petroxolin	0.70	0.46	2.64	2.14	6.34	4.65	11.94	7.22	17.19	9.74
50% colloidal	0.82	0.70	2.57	2.51	6.06	4.39	11.94	6.25	18.02	8.15
50% simple	0.90	1.10	2.00	5.50	5.00	9.20	10.70	13.50	.....	.....
25% U. S. P.	0.50	0.61	1.95	2.10	4.38	4.20	7.50	6.78	9.34 (32 days)	8.47
50% clean	0.20	1.80	1.10	4.50	2.85	7.30	5.40	10.40	.....	.....
5% oleate hard	0.34	0.80	1.25	2.17	2.46	3.39	3.82	4.43	4.98	5.47
5% oleate soft	0.33	0.37	1.00	0.87	1.94	1.53	3.06	2.48	3.93	3.44
5% U. S. P.	0.19	0.71	0.61	1.83	1.21	3.38	2.09	5.25	3.00	6.68
25% colloidal	0.13	0.126	0.50	0.54	1.15	1.17	2.00	1.76	2.75	2.43
2% oleate	0.23	0.50	0.56	1.08	0.98	1.76	1.43	2.79	1.83	3.78

concentration of the element in the ointment base is too low. It probably should be at least from 30 to 50 per cent in concentration to give the required results. The influence of the chemical change of the mercury ointment into the oleate we believe to have been overemphasized in the literature. Does the mercury oleate absorb more readily than the official mercury ointments? This we have been unable to find in our studies on excretion. It therefore matters little in prescribing an official mercurial ointment, from a drug store, whether it is fresh or eight years old. There will be about the same absorption and excretion of mercury from the one as from the other. This we feel is a rather important answer to what has been a mooted question to syphilographers in the past.

One would rather feel from the contention of Fürbringer and Binz that the inunction of colloidal mercury ointments would be more readily absorbed than would ordinary mercury preparations. The small metallic globules might be expected more easily to penetrate the follicles than the

large mercury globules. Nevertheless, we found that the excretion of mercury is no larger with these preparations than with the official ointments. For some reason, however, salivation does seem to be more frequent in some of these cases. This we are as yet unable to explain; it may have been a coincidence. We have already gone on record to the effect that salivation depends on the intensity and on the duration of the excretion of mercury, but that patients hypersusceptible to stomatitis may develop this condition early when the excretion level of mercury is still low. That was true with the colloidal mercury and yet it is singular that the stomatitis developed early in such a large proportion of patients treated with inunction of 50 per cent colloidal mercury. With 25 per cent colloidal mercury, on the other hand, such was not the case.

We do feel that the condition of the teeth, under ordinary hospital care, makes little difference as to the presence or absence of salivation. We are more convinced of this as we follow successive groups of patients under study with mercury preparations.

Mercury in a base of the type of petroxolin, consisting largely of soap, seems to be absorbed and excreted more or less like simple inunction of stronger mercurial ointment when the base is benzoinated lard.

From our study now in press on intensive, or massive weekly simple inunctions of 30 per cent mercurial ointment, using 9 Gm. of metallic mercury to an inunction, we believe we have found a further valuable method of exhibiting the mercury. The excretion of mercury in this method, even using the 30 per cent preparation, is, if anything, higher than with the 50 per cent simple daily inunction, the 50 per cent clean inunction, the 25 per cent simple inunction and the daily instramuscular injections of binbromide of mercury. We believe the method to be of value when daily inunctions are impossible or inconvenient and yet when weekly supervision, or supervision from time to time, by the physician, is necessary.

CONCLUSIONS

1. The absorption and excretion of mercury after inunction is directly dependent on the concentration of the metal in the base. Observations on 5 per cent, 25 per cent and 50 per cent preparations show that the excretion is about in proportion to the concentration in the ointment used.

2. Mercury in an oleate base does not seem to be much more absorbed than in the ordinary benzoinated lard and suet base. Probably there will be as good an absorption from an old mercury official ointment as from a fresh preparation and vice versa.

3. Colloidal mercury ointments show no greater excretion of mercury than official mercury ointments of equal concentration in benzoinated lard. Salivation is possibly more frequent with the colloidal preparations.

4. Fifty per cent mercury in a stiff petroxolin base shows no especial difference in the excretion of mercury from that when simple inunction of 50 per cent mercurial ointment is used.

5. Massive or intensive weekly inunctions of a 30 per cent mercurial ointment, total 9 Gm. metallic mercury, gives an equal or higher excretion of mercury than the simple daily 50 per cent mercurial ointment, 50 per cent clean ointment, or daily intramuscular injections of binbromide of mercury.

ABSTRACT OF DISCUSSION

DR. P. J. HANZLIK, San Francisco: This paper puts the use of mercurial ointment on a more definite basis and shapes the problem of mercury for further study. This has been achieved with the new and highly sensitive quantitative method of estimating mercury used by the authors. I think one may say that the use of methods of precision in studies of the heavy metals—mercury, lead and bismuth, during the past decade or so, has taught us more than the guesswork of centuries.

One of the impressive things is the exceedingly minute concentration of mercury which must be in circulation in the body and suffices in the treatment of syphilis. The concentration appears to be as low as hundred thousandths or millionths of 1 per cent. This reminds us of what has been said of vitamins, that they are the little things in nutrition, the metals being the little things in therapeutics. Dr. Cole and his associates show that a 30 per cent ointment gives about as much excretion of mercury as a 50 per cent ointment, which indicates about equal amounts of mercury in circulation. This points to the choice of the weaker ointment for economic and other reasons. There is the interesting difference between the different bases, which might have been suspected but the objective proof of which was needed. The differences in the fecal and urinary ratios are striking; they appear to be determined partly by the method of administration. For instance, after injection there is more mercury in the urine than in the feces, whereas after inunction the excretion is about the same in both excreta, or there is more in the feces. This difference would not be suspected *a priori,* but there must be a reason for it. The clean inunction method which, I believe, removes a good part of the mercury and leaves the skin clean, still gives a high fecal ratio, though smaller than the dirty inunction; this would suggest other factors, besides the contamination indicated by the authors, causing the high fecal ratios of inunctions.

We know from the work of Padtberg and others that the sodium chloride content of the skin is higher than that of the underlying tissue. Correlating this fact with the results of Garcia, who showed that chlorides mobilizes and increases the amount of mercury in the tissues, is it not conceivable that the skin-chloride acts similarly on inuncted mercury? That is, mercury applied to the skin is rendered more soluble than injected mercury, more is circulated and presumably more would be excreted in the feces. This brings up the interesting questions, whether a salty diet may mobilize mercury, and whether differences in the dietary may explain individual differences in excretion, and perhaps even in antisyphilitic action, of mercury.

DR. A. G. YOUNG, Cambridge, Mass.: So far as the unusual excretion of mercury is concerned in the one patient pointed out by Dr. Cole, it is possible that the patient may have become somewhat febrile, or may have taken a large amount of food high in acid precursors. After the mercury is absorbed, the action in the body will be the same as with other compounds, and I believe the rate of excretion

would be affected by the diet, just the same as in the work we have done. I believe it would be interesting to Dr. Cole, after the patients have ceased to excrete mercury, to put them on a low calcium acid diet, plus ammonium chloride, to determine whether they would not excrete more mercury.

DR. GEORGE W. HARTMAN, San Francisco: I wish to ask whether Dr. Cole considers the intensive inunctions given at weekly intervals of as great value as the daily ones. I should also like to have him repeat the method of inunction used.

DR. HAROLD N. COLE, Cleveland: As to the use of the intensive weekly inunctions, I see no reason why this method cannot be employed as well as the daily inunctions. We use a 30 per cent ointment containing 9 Gm. of metallic mercury, and have it rubbed in by two rubbers for one hour. If desired, it could be rubbed in by one rubber for two hours.

BISMUTH ARSPHENAMINE SULPHONATE (BISMARSEN) IN THE TREATMENT OF SYPHILIS AND OF OTHER SPIROCHETIC INFECTIONS*

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In bismuth arsphenamine sulphonate (bismarsen) a distinct advance has been realized in syphilotherapy, especially since it represents the successful culmination of a long series of chemotherapeutic attempts to combine two such well known spirocheticidal agents as arsphenamine and bismuth in a single compound. It was synthesized by Dr. George W. Raiziss in 1925, and I have had the opportunity of using it since then in a combined clinical and laboratory investigation, the results of which are briefly summarized in this communication.

Stokes and Chambers [1] reported that the toxicity of the drug is low, that reactions are comparatively benign and controllable, and that it is a useful alternate in cases in which other arsphenamines have produced cutaneous and hepatic reactions. They found it especially valuable in the treatment for cardiovascular syphilis, and taken all in all a compound of distinct value in syphilotherapy and especially in the prevention of late syphilis by the simplification and increased effectiveness of the treatment for early syphilis.

O'Leary [2] also had an encouraging experience with it in the treatment of acute syphilis reporting a low incidence of relapses and reactions, although the acute signs of syphilis were slower to disappear than is usual with other preparations of arsphenamine; Tobias [3] stated that it has yielded encouraging results in the treatment of tabes dorsalis.

ADVANTAGES OF INTRAMUSCULAR MEDICATION

Bismarsen is especially interesting from the standpoint of intramuscular medication because of the distinct advantages attached to this route of administration. Greater ease of injection and simplification of treatment, and particularly in the case of children and obese adults, greater freedom from possible toxic reactions, and lower costs are generally emphasized as advantages of intramuscular over intravenous

* Submitted for publication, July 30, 1929.

* From the Research Institute of Cutaneous Medicine.

1. Stokes, J. H., and Chambers, S. O.: Bismuth Arsphenamine Sulphonate, J. A. M. A. **89**:1500 (Oct. 29) 1927.

2. O'Leary, P. A.: Bismuth Arsphenamine Sulphonate, Arch. Dermat. & Syph. **18**:372 (Sept.) 1928.

3. Tobias: Am. J. Syph. **12**:536, 1928.

medication in syphilis but of far greater importance is the question of therapeutic effects. It is becoming more and more evident in chemotherapy that the direct action of a drug on parasites plays but a minor rôle in the mechanism of curative activity and that this indeed is much more likely to be an indirect process calling for the cooperation of the tissues of the host in the production of curative substances in the form of a transformation of the drug in the blood or tissues of the patient with possible stimulation of immunologic resistance. Intramuscular injections have the advantage of slower absorption and slower elimination, and therefore afford more time and opportunity for these essential changes of the drug in the body as well as more time and opportunity for therapeutic agents to reach and penetrate inflammatory tissues of syphilitic infection and *Spirochaeta pallida* itself, especially in the chronic forms of the disease.

It may be expected therefore that intramuscular injections of arsphenamine and neoarsphenamine would be just as effective, although slightly slower in action than equal doses per body weight by intravenous injection; this has been found true in the treatment of syphilis of the rabbit. Were it not for the intolerable pain and disability produced by intramuscular injections of adequate doses of arsphenamine and neoarsphenamine, this route of injection would be the one of choice, except possibly in the treatment of persons with acute cases of early syphilis, when the more rapid although less sustained effects of intravenous medication constitutes an advantage.

But in the treatment of persons who have subacute and chronic types of syphilis intramuscular medication is the route of choice, provided that doses of worth while size and curative activity can be borne by patients without excessive pain and disability. Therefore it is but natural that a coordination compound of bismuth and arsphenamine carrying from 12 to 15 per cent of arsenic and from 23 to 25 per cent of bismuth and capable of repeated intramuscular injection in doses of 0.2 Gm. each without excessive local reactions should engage attention in the treatment of patients with syphilis and other spirochetic diseases. This is particularly true, since in combination therapy it would appear possible to increase the spirocheticidal activities of bismuth and arsphenamne administered together beyond the summation of the effects of the two separately without an increase of toxic effects, or, as stated by Ehrlich, to "march separately, strike combined," the object being to attack the spirochetes simultaneously with bismuth and arsphenamine, and thus to produce a successful result by the combination of the two spirocheticidal substances, each of which alone in the amounts administered may not show a sufficient effect.

PROPERTIES OF BISMARSEN

According to Raiziss,[4] bismarsen is tris (sodium 3-animo-4-hydroxyphenylarseno-N-methyllenesulphonate) dibismuth, corresponding to the empiric formula $C_{21}H_{21}O_{12}As_2Na_3S_3N_3Bi_2$. The bismuth is combined with arsenic in the same manner as silver, gold or platinum in their corresponding coordination compounds of arsphenamine. It is a brownish-yellow, amorphous powder freely soluble in cold water,

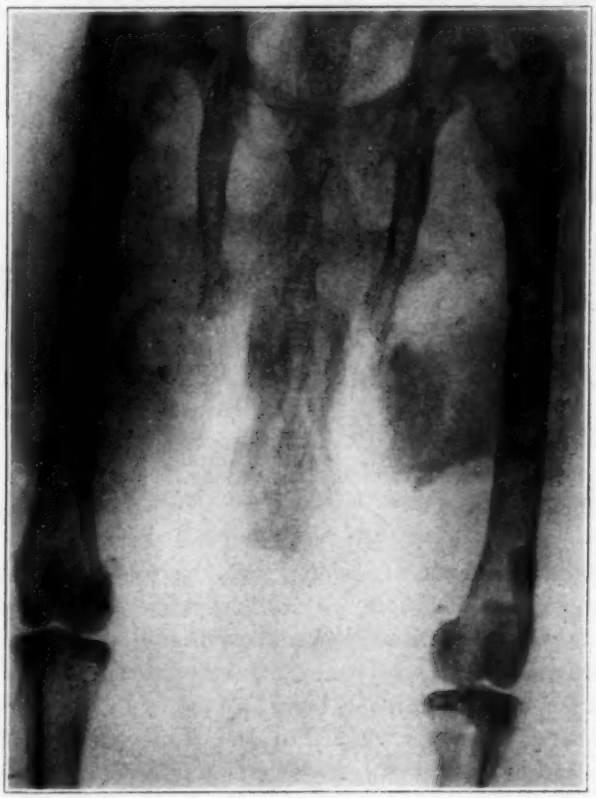

Fig. 1.—Roentgenogram made immediately after the injection of 0.2 Gm. of bismarsen dissolved in 1 cc. of butyn-water into the thigh muscles of a rabbit.

and like other derivatives of arsphenamine cannot be obtained either in crystalline form or entirely free of admixture with inorganic salts.

Tissue Solubility; Absorption and Elimination.—Bismarsen is also tissue-soluble, which is an important matter from the standpoint of absorption. Watery solutions (0.4 per cent) are not precipitated in vitro by sodium chloride, sodium carbonate and bicarbonate, phosphate buffer with a p_H of 6.4 or by defibrinated human blood, blood serum

4. Raiziss: Personal communication to the author.

or watery extracts of muscle. Not infrequently patients receiving intramuscular injections of 0.2 Gm. dissolved in 2 cc. of butyn-water will comment a minute or two afterward on an ethereal taste evidently due to the rapid absorption and diffusion of the arsenic, which doubtless also accounts for occasional "nitritoid" reactions following within a few minutes of injection, and to which further reference will be made.

Rapid absorption is also indicated by the results of roentgenograms. Serial photographs of rabbits receiving injections in the posterior thigh

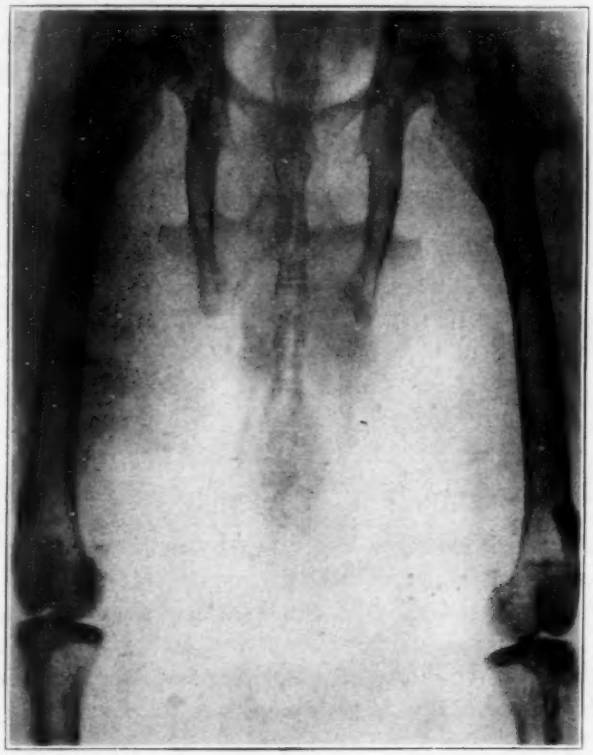

Fig. 2.—The same rabbit shown in figure 1 photographed twenty hours later and showing complete disappearance of the shadow.

muscles of 0.2 Gm. of bismarsen dissolved in 1 cc. of butyn-water have shown complete disappearance of the shadows in from sixteen to twenty-four hours (figs. 1 and 2). O'Leary has observed the complete disappearance of shadows two hours after the injection of 1 cc. of bismarsen solution in the muscles of human beings. Evidently the drug is rapidly diffused in the muscles and does not usually produce as large or as lasting nodosities as sometimes follows the injection of insoluble bismuth salts in oil. Furthermore, microscopic examination of muscles of rabbits and guinea-pigs into which bismarsen has been injected have

not shown any deposition of bismuth because of its tissue-soluble properties, to which further reference will be made.

TOXICITY OF BISMARSEN FOR THE LOWER ANIMALS

(*a*) *Intramuscular Injection.*—Raiziss[4] states that the drug is tolerated by white rats in doses of about 0.5 Gm. per kilogram of weight when injected intramuscularly, but in my tests the maximum tolerated dose has varied with different lots from 0.25 to about 0.4 Gm. per kilogram with a general average around 0.3 Gm.

This low toxicity is probably due in large part to the smaller amount of bismuth than is present in other bismuth compounds, although it is to be remembered that bismarsen also carries about 13 per cent of arsenic. It is interesting, therefore, to compare the toxicity of some other water-soluble bismuth and arsphenamine preparations for the white rat administered by intramuscular injection, and to note that the

TABLE 1.—*Toxicity of Bismarsen for Rats by Intramuscular Injection* *

No.	Weight, Gm.	Dose per Kg.	Days									
			1	2	3	4	5	6	7	8	9	10
1	150	0.200	—**	—	—	—	—	—	—	—	—	—
2	125	0.300	—	—	—	—	—	—	—	—	—	—
3	130	0.400	—	—	—	D						
4	120	0.500	—	D								
5	135	0.600	—	D								

* Ten per cent solutions injected.

** The sign — means survived; D, died.

maximum tolerated doses per kilogram of weight are approximately in ratio to the amount of bismuth or arsenic present in each as follows: potassium tartrobismuthate, 61.3 per cent bismuth, 0.200 Gm.; sodium and potassium tartrobismuthate, 44.3 per cent bismuth, 0.200 Gm.; sulpharsphenamine, from 20.7 to 23.6 per cent arsenic, 0.400 to 0.600 Gm., and bismarsen, 23 per cent bismuth and 13 per cent arsenic, 0.250 to 0.400 Gm.

It will be noted, therefore, that the dose of bismarsen advised in the treatment of patients with syphilis, namely, 0.2 Gm. per adult administered by intramuscular injection and corresponding to approximately 0.003 Gm. per kilogram of weight, is an extremely small dose from the standpoint of toxicity. I have given rabbits as many as forty-two intramuscular injections of 0.003 Gm. per kilogram at four or five day intervals without loss of weight or fatalities, so that it may be stated that bismarsen is well borne by the lower animals when administered by this route.

(*b*) *Histopathologic Tissue Changes.*—Furthermore, microscopic examination of the kidneys, liver, suprarenal glands, spleen, heart and

brain of rabbits, rats and guinea-pigs receiving from six to eighteen intramuscular injections of the compound in this dose (0.003 Gm. per kilogram) have shown but slight or no tissue changes, even after a large number of injections. No changes were detectable in the tissue of the brain, heart, suprarenal glands, spleen or liver after from twelve to thirty-six consecutive injections at four or five day intervals, although after from eighteen to thirty-six doses changes were sometimes produced in the kidneys in the form of cloudy swelling and desquamation of cells of the convoluted tubules.

Larger doses, like 0.03 Gm. per kilogram and corresponding to approximately 2 Gm. per sixty kilograms given by intramuscular injection, or ten times the usual adult dose, produced more profound changes in the convoluted tubules of the kidneys together with cloudy swelling and focal necrosis of the liver when from ten to fifteen doses were given at four or five days intervals. These changes were similar to those described by Lucke and Klauder,[5] and by Lucke and myself[6]

TABLE 2.—*Toxicity of Bismarsen for Rats by Intravenous Injection* *

No.	Weight, Gm.	Dose per Kg.	Days									
			1	2	3	4	5	6	7	8	9	10
1	120	0.025	—**	—	—	—	—	—	—	—	—	—
2	125	0.030	—	—	—	—	—	—	—	—	—	—
3	130	0.035	—	—	—	—	D					
4	120	0.040	—	D								
5	140	0.050	D									

* Five-tenths per cent solutions injected at the rate of 0.5 cc. per 60 seconds.
** The sign — means survived; D, died.

with various soluble and insoluble salts of bismuth; they indicate that bismarsen like bismuth compounds in general is most toxic for the kidneys and next for the liver; it is relatively nontoxic for the brain, heart, suprarenals and spleen.

(*c*) *Intravenous Injection.*—By intravenous injection, the maximum tolerated dose of bismarsen for the rat has been about ten times less, or from 0.03 to 0.04 Gm. per kilogram of weight (table 2). This is about the same toxicity as that of the mercurials flumerin, and mercurochrome-220 soluble, and doubtless bismarsen could be administered by intravenous injection, although this has not been advised, as is true of bismuth compounds in general. The minimal lethal dose of bismarsen or the smallest amount causing death in twenty-four hours has usually varied from 0.04 to 0.06 Gm. per kilogram of weight.

Furthermore, the intravenous injection of bismarsen has caused profound changes in the kidneys and livers of rabbits, rats and guinea-

5. Lucke and Klauder: J. Pharm. & Exper. Therap. **21**:313, 1923.

6. Kolmer: Chemotherapy with Special Reference to the Treatment of Syphilis, Philadelphia, W. B. Saunders Company, 1926, p. 776.

pigs, and constitutes the important objection to this route of administration, as is true of other water-soluble salts of bismuth.

I may state, however, that bismarsen does not cause either hemolysis or agglutination of erythrocytes in vitro, and it does not appear that any part of its toxicity by intravenous injection can be ascribed to either intravascular hemolysis or agglutination. Final dilutions of 1:20, 1:40, 1:60, etc., have caused no hemolysis or agglutination of even washed human erythrocytes deprived of the protective influence of serum; furthermore, these amounts of bismarsen have not produced any demonstrable precipitation of serum in vitro.

LOCAL REACTIONS

In my experience, the intramuscular injection of 0.2 Gm. of bismarsen has usually produced distinctly more local reaction in the majority of patients than has the injection of a similar dose of potassium tartrobismuthate in oil, but no more and usually less than that produced by the injection of 1 grain (0.06 Gm.) doses of mercuric salicylate or 0.4 Gm. doses of sulpharsphenamine. Since the introduction of butyn-water for dissolving the compound, there has been little or no immediate pain; but the late reactions developing about three days later have been less frequent, and abscesses have not occurred in approximately 800 injections.

As is well known, some adults are far below the average in their tolerance for drugs given by intramuscular injection, and these do not bear well repeated injections of bismarsen or sulpharsphenamine, although insoluble bismuth salts may be given. But the great majority of adults and children can be given repeated injections at weekly intervals without excessive reactions or complaints, and tabetic patients bear the injections particularly well, as is true of other compounds given by intramuscular injection to this group of patients.

Local Histopathologic Tissue Changes.—The intramuscular injection of bismarsen produces much less tissue injury than the water and tissue-insoluble salts of bismuth. Indeed it would appear that the maximum injury is due to the arsenic of the molecule rather than to bismuth. The injection of 0.02 Gm. amounts dissolved in 1 cc. of water into the muscles (thigh) of the rabbit and rat has usually produced slight edema followed by Zenker's necrosis of the muscle cells, but little or no infiltration of the injured area with leukocytes; the area of muscle injury, however, has usually been circumscribed by a zone of leukocytes in the midst of swollen muscle fibers, with slight Zenker's necrosis of muscle beyond this zone. As a general rule, tissues removed four or more days after injection have shown the deposition of lime

salts in some of the injured muscle cells (fig. 3) but no deposits of bismuth.

In about seven days new fibrous tissue appears which, within the following two or three weeks, largely displaces those muscle cells that have undergone autolysis and absorption or atrophy, with the production of quiescent scars.

Bismarsen, therefore, produces a larger and more diffuse type of local lesion than insoluble bismuth in the form of various salts of sus-

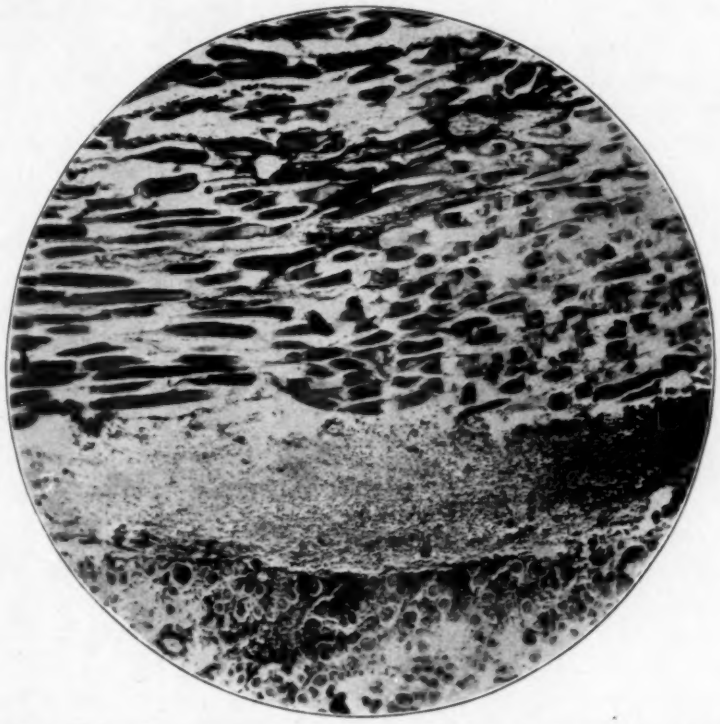

Fig. 3.—Photomicrograph of a section of the thigh muscle of a white rat removed four days after the injection of 0.2 cc. of a 1:10 dilution of bismarsen (0.02 Gm.). The upper part shows edema, partial necrosis of the muscle cells with a slight lime deposition produced by bismarsen; the lower part shows a wall of leukocytes with an adjoining normal muscle.

pensions of the metal itself, but there are much less complete necrosis of muscle and more rapid healing. Injections of the latter in the same dose have usually produced areas of complete and rapid necrosis with deposits of bismuth which have been surrounded by intense zones of degenerating and fragmenting leukocytes (fig. 4); this has usually been followed by fibrosis and encapsulation.

CONSTITUTIONAL REACTIONS

The incidence of constitutional reactions has been low, and those which have occurred were due, in my opinion, in large part to the arsenic in the molecule.

For example, two patients developed hepatitis with jaundice exactly similar to the arsenical jaundice of arsphenamine. Three others developed pruritus, which may have progressed to severe dermatitis had the injections been continued; as it was, none developed exfoliative dermatitis, although I believe that it is advisable to give bismarsen with great caution to any one who has had arsenical jaundice or dermatitis, because it contains enough arsenic to produce recurrent reactions in these susceptible persons. Two patients developed the tingling of fingers and toes that occurs in early arsenical neuritis, which gradually disappeared when the injections were promptly stopped. Two developed mild vasoparetic or "nitritoid" reactions within a few minutes after injection, the flushing and vomiting subsiding in both before they left the office. I have never enountered hemorrhagic encephalitis or severe gastro-

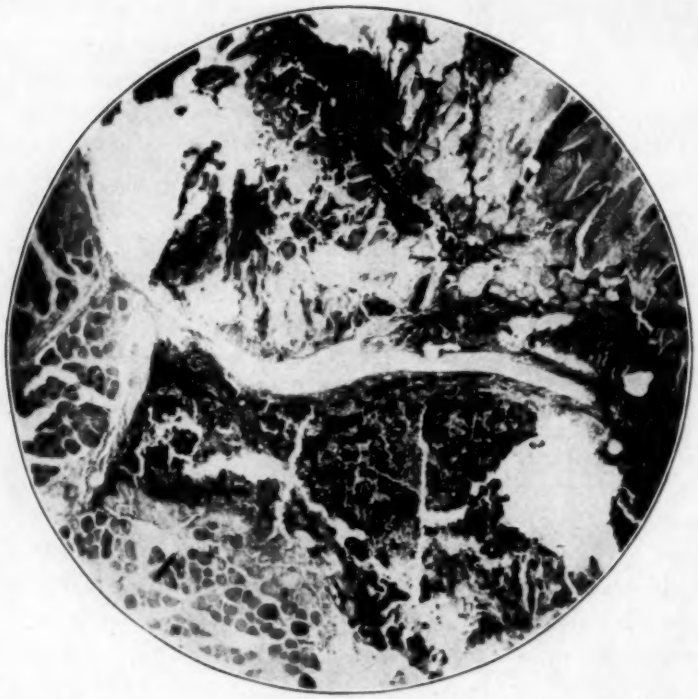

Fig. 4.—Photomicrograph of a section of the thigh muscle of a white rat removed four days after the injection of 0.02 Gm. of potassium tartrobismuthate in oil.

intestinal reactions due to this compound. It has caused the acute exacerbation of lesions in two cases of chronic arsenical eczema.

Siderosis with slight halitosis was observed in six cases after eight or more injections of 0.2 Gm. each had been given; bismarsen, therefore, has been less likely to produce siderosis in my experience than potassium tartrobismuthate, doubtless because of its lower percentage of bismuth. I have never seen severe gingivitis, although in one of my patients a localized ulcerative stomatitis developed at the site of irritation caused by a lower molar tooth. Purpura with aplastic anemia and stomatitis has not developed in any of my patients.

While the urine has been examined as a routine every two or three weeks in all cases, I have rarely observed albuminuria with casts ascribed to the effects of bismarsen; nor have I observed any diuretic effects from the compound in so far as this could be determined in ambulatory patients.

TABLE 3.—*The Trypanocidal Activity of Bismarsen (Kolmer Method) by Intravenous Injection*

No.	Weight, Gm.	Dose per Kg.	Days 1	2	3	4	5	6	8	10	12	14
1	120	0.004	+	+++	++++	D						
2	135	0.006	+	+++	++++	D						
3	125	0.008	+	++	++++	++++	D					
4	150	0.012	—	—	—	—	—	—	—	—	—	—
5	120	0.015	—	—	—	—	—	—	—	—	—	—

TRYPANOCIDAL EFFECTS

The various soluble and insoluble salts of bismuth commonly employed in the treatment of syphilis possess little or no demonstrable trypanocidal activity, but bismarsen has been found to have this property in well marked degree. Of course, a compound devoid of trypanocidal activity may be spirocheticidal, so that the absence of trypanocidal activity does not necessarily mean the absence of curative activity in syphilis by spirocheticidal activity; yet the fact that bismarsen is actively trypanocidal is acceptable evidence of higher parasiticidal power than if it were without this property.

In tests by my method in which white rats infected with *Tr. equiperdium* were employed, the minimal curative dose by intravenous injection has been about 0.012 Gm. per kilogram (table 3) and by intramuscular injection about 0.015 Gm. per kilogram (table 4). By the Voegthin (Hygienic Laboratory) method, the minimal effective dose by intravenous injection has been about 0.02 Gm. per kilogram (table 5) and by intramuscular injection about 0.03 Gm. per kilogram (table 6).

It is interesting to compare the trypanocidal activities of arsphenamine and bismarsen according to the route of administration and their arsenic content. By my trypanocidal method the minimal curative dose of each per kilogram of weight is approximately as follows:

	Arsphenamine (32 per cent of Arsenic)	Bismarsen (13 per cent of Arsenic)
Intravenous injection.....	0.006 Gm.	0.012 Gm.
Intramuscular injection.....	0.004 Gm.	0.015 Gm.

TABLE 4.—*The Trypanocidal Activity of Bismarsen (Kolmer Method) by Intramuscular Injection*

No.	Weight, Gm.	Dose per Kg.	Days 1	2	3	4	5	6	8	10	12	14
1	140	0.005	+	++	++++	D						
2	135	0.010	+	++	++++	++++	D					
3	150	0.015	—	—	—	—	—	—	—	—	—	—
4	120	0.020	—	—	—	—	—	—	—	—	—	—
5	150	0.030	—	—	—	—	—	—	—	—	—	—

TABLE 5.—*Trypanocidal Activity of Bismarsen (Voegthin Method) by Intravenous Injection*

No.	Weight, Gm.	Dose per Kg.	Count Before Injection	Days 1	2	3	5	8
1	150	0.008	100,000	600,000	750,000	++++	D	
2	130	0.010	98,000	400,000	760,000	++++	D	
3	150	0.015	110,000	150,000	—	—	+	++
4	140	0.020	120,000	140,000	—	—	—	—
5	125	0.030	150,600	120,000	—	—	—	—

TABLE 6.—*Trypanocidal Activity of Bismarsen (Voegtlin Method) by Intramuscular Injection*

No.	Weight, Gm.	Dose per Kg.	Count Before Injection	Days 1	2	3	5	8
1	150	0.010	100,000	300,000	600,000	D		
2	150	0.015	140,000	110,000	200,000	++++	++++	D
3	130	0.020	150,000	—	—	—	+	++
4	140	0.030	145,000	—	—	—	—	—
5	150	0.040	110,000	—	—	—	—	—

It will be observed that while the trypanocidal activity of arsphenamine by intramuscular injection is about the same or slightly greater than that by intravenous injection, the activity of bismarsen is slightly reduced by intramuscular injection. This is probably due in part to the slower absorption of the latter.

In intravenous injection, however, when the question of rapidity of absorption does not enter, it is interesting to note that while the arsenic content of arsphenamine is approximately 2.4 times greater than that of bismarsen, the trypanocidal activity of the former is but two times

greater, indicating that the bismuth in the bismarsen molecule probably exerts some trypanocidal activity when associated with arsphenamine in this form of combination therapy, whereas bismuth alone is almost without demonstrable trypanocidal activity.

In my opinion, this constitutes one of the chief points of interest concerning bismarsen in the treatment of syphilis, since it indicates that the administration of the two compounds of totally different origin may increase parasiticidal effects, not only by a summation of the curative activities of each alone but, possibly, by reason of the fact that one may enhance the parasiticidal effects of the other by physicochemical changes.

SPIROCHETICIDAL PROPERTIES IN SYPHILIS OF RABBITS

Similar results have been observed in the treatment of rabbits with syphilis. According to Raiziss, the successive intramuscular injection of from 0.005 to 0.01 Gm. per kilogram causes the complete disappearance of spirochetes from scrotal lesions within two or three days after the first injection, along with complete sterilization of the lymph glands.

The minimal single curative doses in my experiments have been approximately as follows: 0.015 Gm. per kilogram by intravenous injection, and from 0.015 to 0.030 Gm. per kilogram by intramuscular injection (average 0.020 Gm.). By intravenous injection, the minimal curative dose is, therefore, about one-twentieth of the maximum tolerated dose. This amount has always produced a complete disappearance of spirochetes from the acute scrotal lesions, and usually complete sterilization of the inguinal lymph glands.

By intramuscular injection, the minimal curative dose has been about ten to twenty times less than the maximum tolerated dose, and this amount has usually (but not always) resulted in sterilization of the lymph glands.

Compared with arsphenamine the minimum single curative doses per kilogram of weight may be expressed as follows:

	Arsphenamine (32 per cent of Arsenic)	Bismarsen (13 per cent of Arsenic)
Intravenous injection.....	0.014 Gm.	0.015 Gm.
Intramuscular injection.....	0.012 Gm.	0.020 Gm.

It will be observed therefore, that while arsphenamine contains about 2.4 times as much arsenic as bismarsen, its spirocheticidal activity by intarvenous injection is about the same and indicates as in the trypanocidal tests given previously in which the results were much sharper, that the presence of bismuth in the bismarsen molecule apparently enhances in definite degree the spirocheticidal activity in so far as intravenous medication is concerned when differences in the rate of absorption do not occur.

Bismarsen administered by intramuscular injection, however, produces a slower disappearance of spirochetes and healing of testicular lesions of rabbits than do intravenous injections of arsphenamine probably in part owing to the slower absorption of the latter from the muscles. In experiments summarized in table 7 it will be observed that the intravenous injection of arsphenamine in doses of 0.020 Gm. each per kilogram of weight caused a complete disappearance of spirochetes in from sixteen to eighteen hours, whereas the intramuscular injection of a similar dose of bismarsen required from thirty to thirty-six hours, sulpharsphenamine from thirty to forty hours and potassium tartrobismuthate in oil from thirty-two to forty-two hours.

BACTERCIDAL PROPERTIES OF BISMARSEN

Since bacterial contamination may occur during the preparation of solutions of bismarsen for administration, I thought it worth while to determine whether or not the usual solution of 0.2 Gm. dissolved in 2 cc.

TABLE 7.—*The Influence of Bismarsen and Other Compounds on the Rate of Disappearance of Spirochaeta Pallida and Healing of Testicular Syphilis of Rabbits*

Compound	Dose per Kilogram, Gm.	Route of Administration	Time Required for Complete Disappearance of Spirochetes	Time Required for Healing of Testicles
Arsphenamine	0.020	Vein	From 16 to 18 hours	From 5 to 7 days
Sulpharsphenamine	0.020	Muscle	From 30 to 40 hours	From 7 to 11 days
Potassium tartrobismuth	0.020	Muscle	From 32 to 42 hours	From 6 to 10 days
Bismarsen	0.020	Muscle	From 30 to 36 hours	From 6 to 10 days

of butyn-water (1:10 dilution) had any bactericidal effects at ordinary room temperature.

When these amounts were seeded with 0.2 cc. of twenty-four hour hormone broth cultures of *Staphylococcus pyogenes aureus* or *albus* it was found that complete sterilization occurred in less than one minute at room temperature. Similar results were observed with hemolytic and nonhemolytic streptococci. The butyn water alone was without bactericidal activity.

Similar experiments with potassium tartrobismuthate in oil showed that complete sterilization did not occur under exposures of ten to fifteen minutes, so that bismarsen has been found actively bactericidal in vitro, and the solution ordinarily prepared for injection (0.2 Gm. in 2 cc.) actually self sterilizing at room temperature.

BISMARSEN IN THE TREATMENT FOR PRIMARY SYPHILIS

In primary syphilis the intramuscular injection of 0.2 Gm. of bismarsen caused a slower disappearance of spirochetes from chancres than ordinarily occurs after the intravenous injection of 0.6 Gm. of

arsphenamine or 0.9 Gm. of neoarsphenamine. In these cases, dark-field examinations were made three or four times daily between 9 a. m. and 7 p. m. In some cases spirochetes were present at 7 p. m. and absent the following morning, so that the time of disappearance of the organisims can only be approximately accurate:

CASE 1.—A man, aged 23, who weighed 142 pounds (64 Kg.) had a six day lesion. The spirochetes disappeared in about thirty-six hours.

CASE 2.—A youth, aged 19, who weighed 129 pounds (59 Kg.) had a four day lesion from which the spirochetes disappeared in about 120 hours.

CASE 3.—A man, aged 41, weighing 162 pounds (74 Kg.) had an eight day lesion from which the spirochetes disappeared in about seventy-two hours.

CASE 4.—A man, aged 32, weighing 146 pounds (66 Kg.) had a four day lesion from which the spirochetes disappeared in about fifty-four hours.

In these four cases the average time of disappearance of spirochetes was a little more than seventy hours. Stokes and Chambers have reported twenty-nine hours and O'Leary seventy-five hours.

All of these four cases yielded negative Kolmer-Wassermann reactions at the time of the first treatment. Each patient received four courses of ten injections each (0.2 Gm. per dose at from five to seven day intervals) or a total of forty injections. All have been under observation for periods varying from eleven months to three and one-half years; none have so far shown positive complement-fixation or precipitation reactions; none have shown detectable clinical relapses, and none have shown spinal fluid changes. All were tested after the fourth course.

While the disappearance of spirochetes and healing of the lesions occurred more slowly than is usually observed after the injection of the arsphenamine, yet it is to be remembered that the dose of 0.2 Gm. administered by intramuscular injection (with slower absorption) is from three to four and one-half times smaller than the maximum doses of arsphenamine and neoarsphenamine administered by intravenous injection, and under these conditions more rapid spirocheticidal action is not reasonably expected and was not less prompt in my experience than follows the intramuscular injection of from 0.2 to 0.3 Gm. of sulpharsphenamine or 0.2 Gm. of three other bismuth compounds.

BISMARSEN IN THE TREATMENT FOR SECONDARY SYPHILIS

Mucous patches and condylomas also showed slower healing and disappearance of spirochetes following intramuscular injections of 0.2 Gm. bismarsen every five to seven days than intravenous injections of 0.9 Gm. of neoarsphenamine at the same intervals; macular and papular syphilis also disappeared somewhat more slowly. It would appear, therefore, that bismarsen is not the drug of choice in the treatment for the acute early lesions or recurrences of syphilis when rapid disinfection of

the lesion is required unless intravenous medication is impossible because of difficult veins. However, the intravenous injection of arsphenamine or neoarsphenamine is rarely contraindicated in primary and secondary syphilis, in my experience, because either compound is usually extremely well borne in these stages.

All of seven cases showed strongly or very strongly positive Kolmer-Wassermann and Kahn reactions before treatment was begun. Two patients were serologically negative two weeks after the second course (total of twenty injections); three were negative after the third course (thirty injections), while two were weakly positive (2 — — — —) after the fourth course (forty injections). Both became negative later following a combination therapy of neoarsphenamine given intravenously and potassium tartrobismuthate intramuscularly. None have so far showed serologic or clinical relapses. All but one showed negative spinal fluid changes when examined after the first negative blood reaction; this one case showed fourteen cells, a weakly positive Pandy reaction, a colloidal gold curve of 0013100000 and a 3i — — — Kolmer-Wassermann reaction (moderately positive), but was asymptomatic.

BISMARSEN IN THE TREATMENT FOR CHRONIC SYPHILIS

This has constituted my largest group and has included Wassermann positive clinically quiescent and Wassermann positive clinically active cases. But despite the fact that I have used bismarsen for almost four years, it is still difficult to express the results in a definite manner with approximate scientific accuracy because of the many years required for evaluating any drug or system of treatment in terms of the ultimate fate of the patient. But during these four years I have gathered a favorable impression of bismarsen for these reasons:

1. I believe that the treatment for chronic syphilis (active or concealed) should always begin with intramuscular injections in order to avoid the acute exacerbations of manifest or concealed lesions sometimes following intravenous injections of the arsphenamines. This has been particularly true in the treatment for cardiovascular syphilis. Since bismarsen is both water and tissue soluble with higher spirocheticidal properties than mercury or insoluble bismuth componds, it has proved an excellent compound in my experience for those persons who bear well with intramuscular injections. Among those who have shown excessive local reactions, my next choice has been a water-soluble and tissue-soluble bismuth alone or an insoluble salt suspended in oil.

2. Furthermore, the commencement of treatment for chronic syphilis with intramuscular injections of bismarsen has had the advantage of determining the tolerance of the patient for arsenic, which is particularly advisable when treatment is resumed after a long rest period when hypersensitiveness may have been induced by preceding arsenical therapy.

3. It has been a safe compound for testing the tolerance of patients for arsenic who have had and have recovered from such arsenical injuries as pruritus, tingling and numbness (of early arsenical neuritis) and jaundice (presumably arsenical). In my experience bismarsen has sometimes produced a recurrence of these, so that I cannot subscribe to the opinion that it is entirely safe after an attack of dermatitis or jaundice, but the recurrent lesions after bismarsen have always been mild although sufficient for warning.

4. It has yielded good tonic effects (probably due to the arsenic), so important in chronic syphilis and especially in tabes dorsalis, with improvement in weight, appetite and energy and increase of hemoglobin and erythrocytes.

5. It has afforded a form of true combination therapy which I believe has a particular field of usefulness in the treatment for chronic syphilis as previously discussed.[7]

It has not caused as rapid healing of such external lesions as gummas and periostitis of the nasal bones and tibia, chronic cutaneous syphilids, etc., as have intravenous injections of arsphenamine, but healing has been generally prompt and satisfactory. It has frequently afforded gradual relief from the lightning pains of tabes and especially from the headaches of syphilitic meningitis.

I believe that bismarsen has a place of particular usefulness in the treatment for Wassermann-fast cases of syphilis, probably because combination therapy is particularly indicated in this group which constitutes the despair of so many physicians engaged in the treatment for syphilis. I am among those who regard persistently postitive complement-fixation and precipitation reactions as evidence of persistent syphilitic infection even in the absence of demonstrable lesions, and I believe that it is necessary to administer at least two courses of treatment a year to the unfortunate victims in order to maintain the so-called latency as long as possible. For this purpose I believe bismarsen constitutes a valuable compound, and I have been so frequently surprised by the gradual reduction of serologic reactions to negativity in cases regarded as Wassermann-fast that I no longer regard this state to be as frequent or as difficult to influence as formerly.

BISMARSEN IN THE TREATMENT FOR CONGENITAL SYPHILIS

Five children, varying in age from 2 to 11 years, have stood intramuscular injections of bismarsen remarkably well. I have given weekly doses of 0.1 Gm. to three children of 6 years of age or less, and 0.2 Gm. at a time to the older ones. Two patients presenting chronic interstitial

7. The Combination Chemotherapy of Syphilis, J. Chemotherapy, to be published.

keratitis as the prominent manifest lesion have had four courses of ten injections each at this writing; the ocular lesions have almost entirely disappeared with a great improvement in weight and general health, but the Kolmer-Wassermann and Kahn reactions are still moderately positive. It is my impression at present that bismarsen may have a special field of uefulness in the treatment of congenital syphilis, especially in the case of children under 4 years of age among whom intravenous therapy is ordinarily difficult, not only because of its spirocheticidal properties but likewise by reason of the tonic effects of the drug.

BISMARSEN IN THE TREATMENT FOR PULMONARY SPIROCHETOSIS

Two cases of pulmonary spirochetosis presenting profuse hemorrhagic bronchial secretions showing enormous numbers of spirochetes in direct smears responded promptly to intramuscular injections of 0.2 Gm. of bismarsen every five days. Both patients were debilitated men. After the third injection the amount of secretion became progressively less, with cessation of hemorrhages and a great diminution of spirochetes. These effects were not as prompt as I observed in a third patient receiving intravenous injections of neoarsphenamine, but it is interesting to note that bismarsen is capable of exerting spirocheticidal effects in pulmonary spirochetosis.

BISMARSEN IN THE TREATMENT FOR VINCENT'S ANGINA

It is my impression that intramuscular injections of bismarsen may likewise be effective in the treatment of patients with extraordinarily severe cases of Vincent's angina. In one case occurring in an extremely obese woman, aged 41, who was seen in consultation and whose life was threatened by an unusually severe infection involving the tonsils, soft palate, buccal mucosa, gums and lips and to whom the attending physician could not give intravenous injections of arsphenamine or neoarshenamine, it appeared that intramuscular injections of 0.2 Gm. every three days for a series of seven injections gradually turned the tide to recovery. Quite a variety of local agents, including freshly prepared sodium perborate, had been previously tried but had failed to check the infection.

Since then I have used bismarsen in five additional cases of unusual severity occurring in institutional children, giving 0.1 Gm. by intramuscular injection every five days combined with the local application of 2 per cent solutions of arsphenamine in 50 per cent glycerin twice a day and frequent swabbings or washings with freshly prepared sodium perborate; it is my impression that the intramuscular therapy aided materially in bringing these infections under control although they are

indicated only in cases of unusual severity or chronicity in which local measures alone have failed.

SUMMARY

1. Bismuth arsphenamine sulphonate (bismarsen) is a compound of particular interest and value because it combines the advantages of intramuscular and combination therapy especially in relation to the treatment for chronic syphilis.

2. It is both water-soluble and tissue-soluble and is rapidly absorbed from the muscles.

3. Its maximum single tolerated dose by intramuscular injection in rats varies from 0.25 to about 0.43 Gm. per kilogram of weight, with an average of 0.400 Gm. As the adult dose is 0.2 Gm. or about 0.003 Gm. per kilogram, the amount ordinarily administered at one time is about 100 times less the maximum tolerated dose for the rat.

4. Its maximum tolerated dose for the rat by intravenous injection is about the same as that for mercurochrome-220 soluble and flumerin, namely, from 0.03 to 0.04 Gm. per kilogram of weight.

5. It does not cause the hemolysis or agglutination of washed or unwashed erythrocytes or the precipitation of serum in vitro, and it would appear that no part of its toxicity by intravenous injection is ascribable to intravascular hemolysis or agglutination.

6. The intramuscular injection of from six to eighteen doses of 0.003 Gm. per kilogram at four or five day intervals caused no histopathologic changes in the brain, heart, spleen, kidneys, liver or suprarenal glands of the rat, guinea-pig or rabbit. From eighteen to thirty-six consecutive doses sometimes produced slight cloudy swelling and desquamation of cells of the convoluted tubules of the kidneys. Larger doses like 0.03 Gm. per kilogram, corresponding to 2.0 Gm. per sixty kilograms, produced more profound changes in the liver and kidneys when from ten to fifteen injections were given at five day intervals.

7. The intramusuclar injection of 0.2 Gm. of bismarsen dissolved in 2 cc. of butyn-water has caused little or no immediate pain, but the late local reactions have been usually more severe than those produced by 0.2 Gm. doses of potassium tartrobismuthate in oil, although usually less than produced by 1 grain doses of mecuric salicylate or 0.4 Gm. doses of sulpharsphenamine. Some patients, and especially women, could not stand repeated injections of the compound. Abscesses did not occur in approximately 800 injections. Nodosities were of exceptional occurrence and disappeared much more rapidly than in the case of injections of insoluble mercury or bismuth compounds.

8. The intramuscular injection of bismarsen produces much less necrosis of muscle than do injections of insoluble compounds in oil.

9. The incidence of constitutional reactions has been low.

10. Bismarsen should be given with caution to persons who have had dermatitis and jaundice, and its administration should be stopped immediately on the recurrence of signs and symptoms.

11. Bismarsen possesses a high degree of trypanocidal and spirocheticidal activity. Since bismuth alone is almost without trypanocidal effects, it would appear that the parasiticidal effects are due largely to the arsenic in combination with the bismuth.

12. Bismarsen (0.2 Gm. dissolved in 2 cc. of butyn-water or a 1:10 solution) is rapidly bactericidal, which reduces the chances of infection during administration.

13. Bismarsen by intramuscular injection in rabbits with acute syphilitic orchitis in doses of 0.020 Gm. per kilogram produced a slower disappearance of *Spirochaeta pallida* than did intravenous injections of arsphenamine in the same dose, probably because of slower absorption.

14. In four cases of primary syphilis the intramuscular injection of 0.2 Gm. of bismarsen caused the disappearance of spirochetes in from 36 to 120 hours. These lesions, however, as well as the lesions of the skin and mucous membrane of the secondary stage, disappeared more slowly than is ordinarily observed after the intravenous injection of from 0.4 to 0.6 Gm. of arsphenamine or 0.9 Gm. of neoarsphenamine.

15. Bismarsen has proved especially valuable in the treatment for chronic syphilis because (*a*) it affords a means of avoiding Jarisch-Herxheimer reactions; (*b*) it exerts greater spirochetical effects than mercury or insoluble bismuth compounds; (*c*) it has the advantage of safely testing the tolerance of patients for arsenic who have previously had arsenical treatment or accidents; (*d*) it has tonic effects, and (*e*) it represents a true form of combination chemotherapy.

16. Bismarsen would appear to have a special field of usefulness in the treatment for congenital syphilis, and particularly in children of 4 years of age or less to whom intravenous medication may not be given.

17. Bismarsen has yielded encouraging results in the treatment for pulmonary spirochetosis and in severe cases of Vincent's angina.

THE GENERALIZED KERATOTIC NEVUS*

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Knowledge concerning the histologic construction of the generalized nevus is as yet imperfect. In the exact clinical and microscopic examinations of patients who come collectively for observation, one therefore encounters sometimes manifestations that are peculiar and in general even unknown, and that seem to correspond to definite clinical forms. That fact holds good also for the following communication.

REPORT OF CASE

Several years ago, a postal clerk, aged 60, appeared at the dermatological division of the Krankenhaus der Stadt Wien for an examination. He showed, as an incidental observation, a generalized unilateral keratotic nevus only slightly developed and extending over one half of the body (fig. 1). On the right side of the back, over the right shoulder and posterior axillary fold, in the loin and over the right half of the nates were seen nodules follicularly placed, partly in groups and partly single, and arranged lineally or in rows. The primary efflorescence was hard and dark brown. The relief corresponded to a widened follicle opening, filled up with horn masses. Most of these follicles on being scratched or removed by scratching showed stunted lanugo hairs. Where these nodules merged into groups, the surface was rough. Some efflorescences gave the impression of a psorospermosis follicularis, Darier. Over the right spina iliaca anterior superior larger plaques were present. Their color was darker and their keratosis was more pronounced. Here the condition reminded one almost of a lichen ruber corneus; however, in this relatively small plaque the lineal arrangement could also be observed distinctly. On the ulnar side of the right arm were similar efflorescences which were small and arranged in groups longitudinally. Inflammation of any sort was absent. Diagnostically, the clinical picture had only one meaning.

Histologic examination disclosed a peculiar and characteristic condition (figs. 2 and 3). The nodules corresponded to circumscribed hyperkeratotic areas which apparently regularly formed part of a follicle opening. The follicle, nevertheless, was not normally formed but was enlarged and troughlike. Its walls were high, so that the papillae which lay along its side appeared drawn out though small. On the sides, its epithelium was formed only by a few cell layers. The floor of this bowl-like depression was formed by an epithelium more than twice the normal thickness and showed the most important changes in the cell connections which overlay the basal layer. The whole depression was filled with horn masses. Almost always, a lanugo hair follicle was discharged from the floor of the depression. While the upper wall which surrounds this depression showed normal epithelium, the change in the epidermis began at a point half way up the wall. Even if the germinal layer appeared normal at first glance, nevertheless, attention was drawn to the fact that here also in the excised section of skin through the

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* From the Dermatological Section of the Krankenhaus der Stadt Wien, Service of Prof. Dr. Otto Kren.

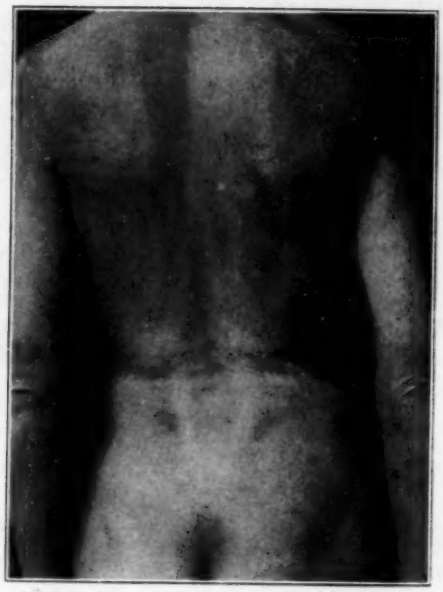

Fig. 1.—Unilateral distribution of nevus from shoulder to nates.

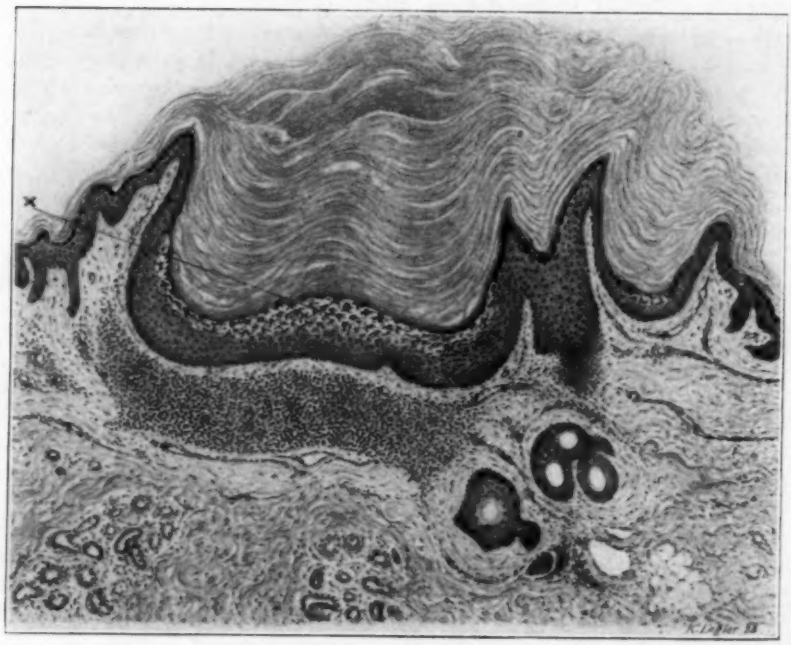

Fig. 2.—Section through the nodule, showing widened and depressed follicle covered with very thick horny layer. At *x* can be seen degenerative changes in the epidermis.

valley-like widened follicle, the pigment, which otherwise was rich, was missing in the germinal layer. Microscopically, that appeared to be the only change. Biologically, however, not only was there a disturbance shown in the pigment formation, but there was also another severe disturbance present in this layer which could not be recognized microscopically but could be inferred from the life cycle of the cells in this layer; for already in the deeper layers of the stratum spinosum, abnormal manifestations of life processes appeared; namely, degeneration forms of the epithelial cells which pointed to disturbances in the embryologic life—a certain dysgenesis.

The first and second layers following the basal layer in the stratum spinosum appeared normal; however, from the third to the fourth cell layers upward, one could already discern perceptible signs of a process of degeneration. An orderly cell structure could not be considered; the nucleus and protoplasm were changed. The nuclei took little strain; often they lay only in cavities or protoplasm-empty sacks. The protoplasm was vacuoled or transformed into numerous more or less clumpy, finely divided or oval masses which stained fairly intensively with eosin

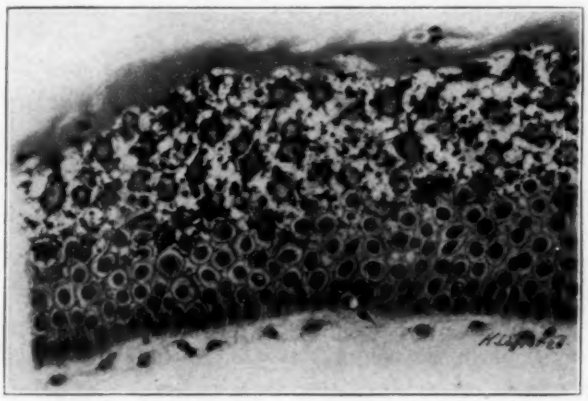

Fig. 3.—Section through the base of follicle at *x* in figure 2, showing more detailed changes in cells (high power).

and which corresponded to degenerated hyaline cell bodies. Such protoplasm lay enclosed yet in cell membranes or free in this stratum. Moreover, in the area of the stratum spinosum, which here no longer deserved the name, round and cleft-like gap formations arose in which one could see the aforementioned hyaline balls and particles occurring singly or in groups. Besides, structures arose here which took the nuclear stain most intensively. The upper half of the epithelium was densely filled up with such structures. They were small masses, from the size of nucleoli to that of large flakes, and were round or shredlike; these lay irregularly in a completely destroyed tissue. The largest masses, often confluent, lay around degenerated nuclei and the remains of nuclei, winding themselves around in a cloaklike fashion and sending out processes into the adjacent area. Between the cell remains and the formerly mentioned balls and granules which were eosin-staining remnants of protoplasm, one saw numerous such particles which were small and darkly stained and also masses that were formed into short threads which in places hung together under one another, and which formed the principal part of the upper layer. Often the darkly stained masses were so large that one saw a cell, its shape preserved, completely filled up with numberless confluent

granules of this kind. Occasional processes of these bulky structures communicated with processes of other similar structures. These communicating threads also carried clublike swellings. According to appearance and staining, these unformed structures belong to the keratohyaline layer.

On this layer of greatest disorder the horny stratum followed abruptly. It was hyperkeratotic and attained a thickness many times the normal, especially as it filled up the depression of the hair follicle opening and manifested itself as an elevation. In some places the hyperkeratosis was firmly united; in other places one could see it in dissolution. With the van Giesen stain it became a dark yellow to a light orange red; with the Gram stain, mostly blue. In this, remnants of nuclei were perceptibly entirely isolated.

The connective tissue was normal as far as a lymphocytic zone under the epithelial change. It was separated from the rete by a narrow border which was formed of connective tissue cross fibers.

External to the change in the epithelium, the rete and derma were normal; there, the pigmentation in the basal layer was a little increased.

In some places the changes lay close together, these corresponding to large clinical plaques.

Thus, a unilateral generalized hyperkeratotic nevus was exhibited histologically as an epithelial nevus. The malformation, which was present only in island form, was transferred to the cells of the germinal layer. Already in the second and third layers of the stratum spinosum most of the cells were degenerating; their protoplasm disintegrated into crumblike flakes; their nuclei prematurely lost their staining ability. Only occasional ones showed a longer resistance to the disintegrating process. Normal keratohyalin could no longer be manufactured. In its place arose unformed crumblike and threadlike structures, behaving like keratohyalin, which lay in compact masses around the remaining nuclei or were embedded between cell remnants and apparently hyaline flakes. Nevertheless, from these irregular masses a horny layer developed to an excessive degree, i. e., hypertrophically; morphologically, and in staining character, this layer was apparently normal. The expiration in the life cycle of the epidermis cell took place in an abnormal manner, but led to an apparently normal end-product. The chemical process taking place here is not clear; so far as is known, it is more than a chemical process.

COMMENT

In the literature the reports of two similar cases were found. The most recent case was reported by Randak,[1] Riehl[2] and finally Arzt.[3] A girl, aged 5, had brown wartlike elevations, which were arranged

1. Randak: Ber. Wien. Dermat. Gesellsch. Sitzg. **5**:22, 1924; Zentralbl. f. Haut- u. Geschlechtskr. **13**:337, 1924.

2. Riehl: Ber. Wien. Dermat. Geschelsch. Sitzg. **6**:5, 1924; Zentralbl. f. Haut- u. Geschlechtskr. **14**:35, 1924.

3. Arzt: Wien. med. Wchnschr. **7**:10, 1926; Zentralbl. f. Haut- u. Geschlechtskr. **22**:68, 1926.

lineally and localized unilaterally. The left axilla, left side of the trunk, left half of the nates, and left thigh were involved. The histologic construction was identical with that of the present case. Along with a simultaneous vacuolization of the cell protoplasm the picture was dominated by an extraordinary multiplication of the granules in the keratohyaline layer—coarse, clumsy, often extraordinarily large flakes and also fine particles which stained intensively with the nuclear dye. On the areas of excessive development a normal rete malpighi was completely absent, so that at times only a single layer of normal construction remained—the basal layer.[3]

At a meeting of the Wiener-Dermatologische Gesellschaft on June 5, 1924, Riehl demonstrated a section of this. In the discussion, Kyrle designated the process of cornification as a "unicum," a solitary case.

Gassmann,[4] however, in his monograph on "Ichthyosis and Ichthyosis-Like Diseases" had previously described a similar case. Histologically, he observed in the rete, almost over the basal layer, marked signs of degeneration which involved nucleus and protoplasm. The latter lay in part as a noticeable homogenous mantle around the nucleus; in part, divided itself in the cell into crumblike, irregular masses. In the higher cell layers this substance arose in small particles and little shreds, and later, as larger lumps; the cells became inflated and showed vacuoles. The nuclei shrank to star-shaped forms or became inflated and lost their staining chromatin framework. Approximately, one-half the width of the stratum mucosum was occupied by a layer in which were found granular particles which were stained intensively dark with hematoxylin. These were small and irregular but larger than normal keratohyaline particles. Their form was also comma or threadlike, often with nodular swellings. They were placed in the periphery of the cell or within the protoplasm masses mentioned. These granules and masses were present in large quantities. An additional, but not a clearly visible, picture along with the description of the microscopic appearance allows one to recognize that in Gassmann's case, the changes present were identical with those in the case of Randak, Riehl and Arzt and in mine. Clinically, Gassmann's case corresponded to a nevus hyperkeratoticus hystriciformis systematicus which was localized symmetrically on both sides of the body but arranged in rows.

CONCLUSIONS

In the clinical picture and cellular construction the two cases described have so much in common with the case mentioned in the

4. Gassmann: Ichthyosis and Ichthyosis-Like Diseases, Arch. f. Dermat. u. Syph., 1904, supplement.

beginning that one cannot but draw the conclusion of the existence of a unity. The single difference lies in the intensity of the progress made. The case of Gassmann's represents the most pronounced bilaterally localized nevus keratoticus, while the present case represents an abortive form. The case of Randak, Riehl and Arzt and the case which I observed are to be considered as nevus keratoticus striatus unius lateris, while in Gassmann's case the growth appears to be arranged segmentally. However, that does not seem to be an essential difference; clinically and in the lineal arrangement the cases are identical. In the same way the pictures correspond in their microscopic appearances.

It seems that the described histologic appearance belongs to an altogether definite clinical picture corresponding to a nevus that is unilateral or, more seldom, symmetrically generalized. Clinically, the primary efflorescences, which are similar to comedo or psorospermosis, are apparently characteristic.

Therefore, there are generalized, hyperkeratotic, hystriciform nevi which are recognizable microscopically as epithelial nevi by a production of keratohyalin that is characteristic, i. e., by a peculiar change in the epidermis.

CUTANEOUS NEUROMA *

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My purpose in this paper is to submit a case presenting all the features essential to the diagnosis of cutaneous neuroma occurring in a patient having tuberculosis.

Because of the rarity of cases observed, neuroma cutis has meant many things to many persons. Wood's [1] "subcutaneous painful tubercles," Rump's [2] "fibroid tumors of subcutaneous nerves," the so-called false neuromas of Virchow [3] and Darnall's [4] "plexiform neuromas" have all been reported as neuroma cutis.

The term itself, however, limits one to those conditions which deal with growths containing abnormal nerve elements and having their location and development in the true skin. The subcutaneous nodules mentioned, together with the "neurofibromas" of Recklinghausen, and the nodules of nerve tissues springing from amputated nerves will therefore not be included under this title.

Duhring,[5] Kosinski,[6] Heidingsfeld,[7] Little [8] and Duemling [9] each reported a separate case that has been accepted as true neuroma cutis.

In addition, Verneuil [10] reported a dissecting room case of myoma cutis in which nerve fibers were present in such abundance that the diagnosis of neuroma could be made almost as well as that of myoma.

In 1893, Cavafy reported to the Dermatological Society of London a case of extremely tender multiple tumors on the back of a woman, which, in Hartzell's opinion, was neuroma cutis.

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* Submitted for publication, Aug. 27, 1929.

* Read before the Section on Dermatology and Syphilology at the Eightieth Annual Session of the American Medical Association, Portland, Ore., July 12, 1929.

1. Wood, W.: Tr. Med.-Chir. Soc. Edinburgh **3**:29, 1829.
2. Rump: Arch. f. path. Anat. u. Physiol. **80**:177, 1880.
3. Virchow: Die Krankhaften Geschwülste **2**:150, 1864.
4. Darnall, W. E.: Multiple Neuromata of the Skin, J. A. M. A. **47**:1810 (Dec. 1) 1906.
5. Duhring, L. A.: Painful Neuroma of the Skin, Am. J. M. Sc. **66**:413, 1873.
6. Kosinski: Centralbl. f. Chir., 1874.
7. Heidingsfeld, M. L.: Neuroma Cutis (Dolorosum), J. A. M. A. **61**:435 (Aug. 9) 1913.
8. Little, E. G.: Brit. J. Dermat. **31**:102, 1919; Proc. Roy. Soc. Méd., Section Dermat., 1919, p. 35.
9. Duemling, W. W.: Cutaneous Neuroma, Arch. Dermat. & Syph. **19**:226 (Feb.) 1929.
10. Verneuil: Am. J. M. Sc., July, 1874.

The authors of the "American Textbook of Pathology" [11] believe that "the multiple dermal neuromas found by Knauss [12] in children can be included in the list of neuroma cutis." Heidingsfeld noted that "of the fourteen cases of well-defined myoma cutis which have been

Fig. 1.—This illustration shows the type of acanthosis and the high position of the nerve trunks in the subpapillary region. There is a broad trunk winding upward at the left and a transversely sectioned one in lower right hand corner.

reported, nine were painful and in some of the cases nerve abnormalities were noted."

11. Ohlmacher, A. P.: Tumors, in Hektoen, Ludvig; and Reisman, David: American Textbook of Pathology, Philadelphia, W. B. Saunders Company, 1901, pp. 175, 194.

12. Knauss: Virchows Arch. f. path. Anat. **153**:29, 1898.

If these possible twelve additions to the five cases more accurately reported are conceded, the condition may still be one of the rarest known to dermatology.

Duhring's report and description were published in 1873, his clinical diagnosis being tuberculid. The lesions were discretely and irregularly disseminated over the left arm and shoulder of a man, aged 70. They consisted of split pea-sized, firm, purplish, flattened tubercles, which were firmly incorporated in the skin. Paroxysmal pain constituted the

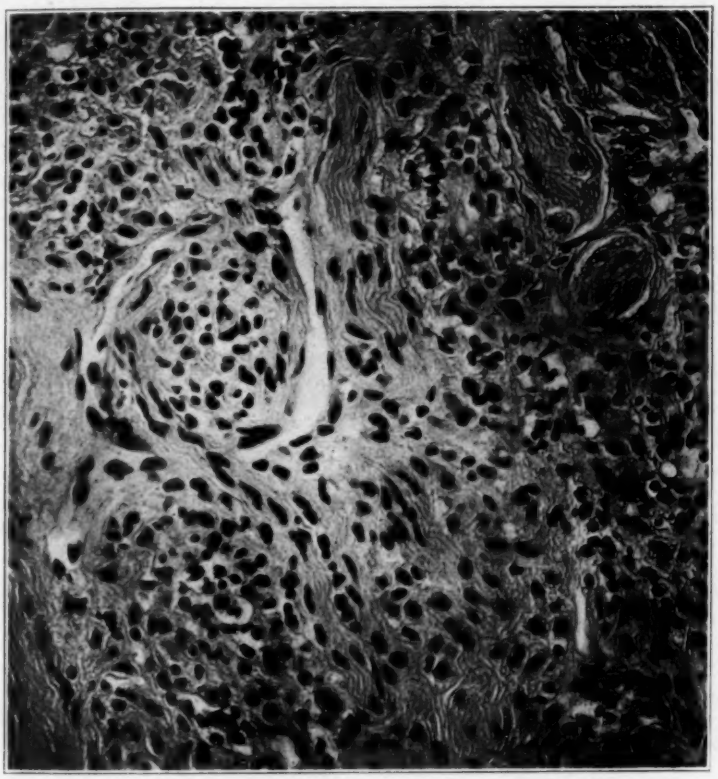

Fig. 2.—Infiltration around and near nerve trunk, polymorphonuclears and fibroblastic hyperplasia being included in the infiltrate.

distressing feature, but did not manifest itself until three years after the tubercles had begun to form.

Microscopic examination [13] revealed the growth to be made up of a connective tissue stroma interwoven with numerous nonmedullated nerve fibers.

Kosinski's case was similar to Duhring's with the lesions, which were later painful, limited to one leg and buttock. His clinical diagnosis was also tuberculid, and the microscopic diagnosis was neuroma.

13. De Schweinitz, G. E.: Am. J. M. Sc. **82**:435, 1881.

Little does not record a clinical diagnosis, but the description of the lesions would suggest tuberculid—hundreds of small, bluish-red, hard nodules, split pea-sized, in the substance of the skin. A section showed that the bulk of the tumors consisted of nerves.

Heidingsfeld's case presented a solitary encapsulated nodule which developed subsequent to an injury and was painless for twenty years. His clinical diagnosis was myoma and the microscopic diagnosis, neuro-endothelioma.

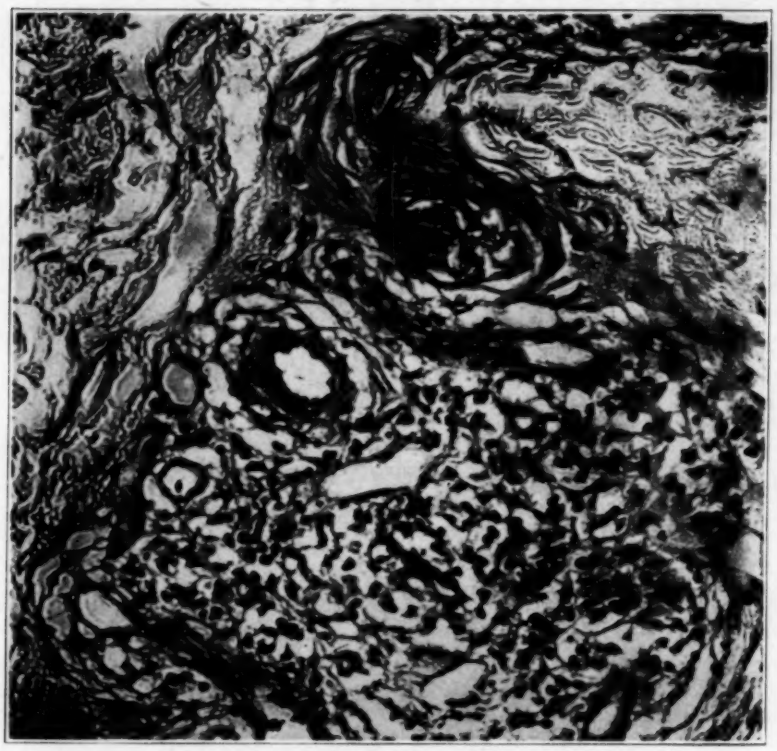

Fig. 3.—Cellular infiltrate, including polymorphonuclears, adjacent to nerve trunk; Giemsa stain.

Duemling's patient presented a single palm-sized lesion of the breast, which was entirely painless for the three months of its duration. The clinical diagnosis was spontaneous keloid or "cancer en cuirasse." The microscopic diagnosis was neuroma.

REPORT OF CASE

History.—M. J., a colored woman, aged 37, said that as a young girl she was greatly troubled with distressing and prolonged "colds," which were intermittently present between the ages of 18 and 25; after that she gained in weight and

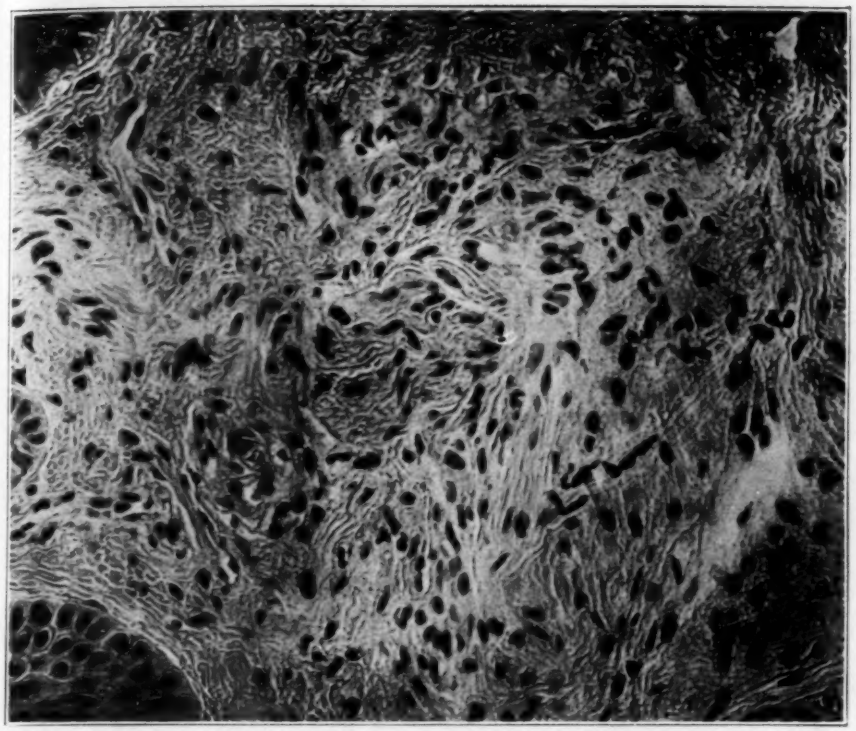

Fig. 4.—Formative nerve trunk in center. Several medullated fibers in center distinguished as clear way slits extend perpendicularly.

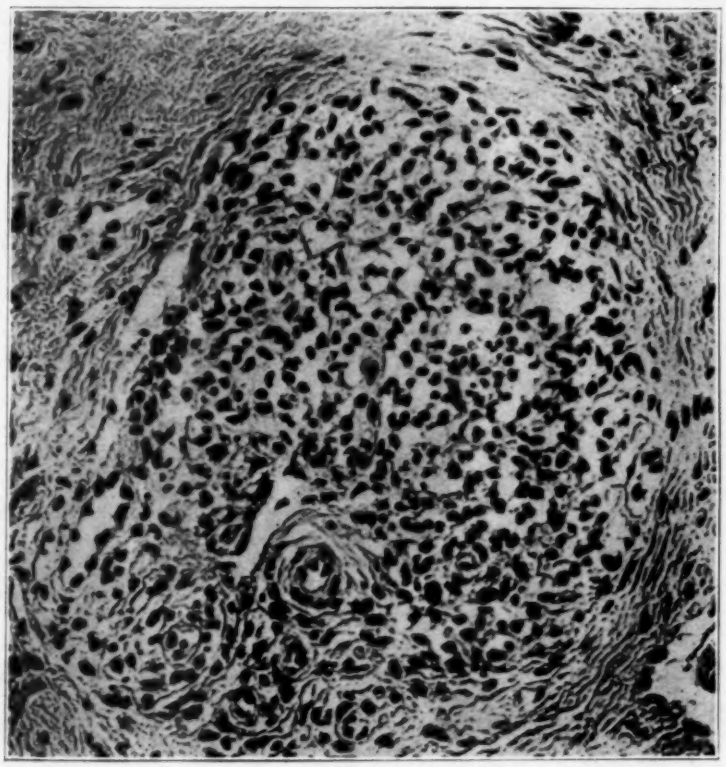

Fig. 5.—Round cell infiltration immediately under epiderm.

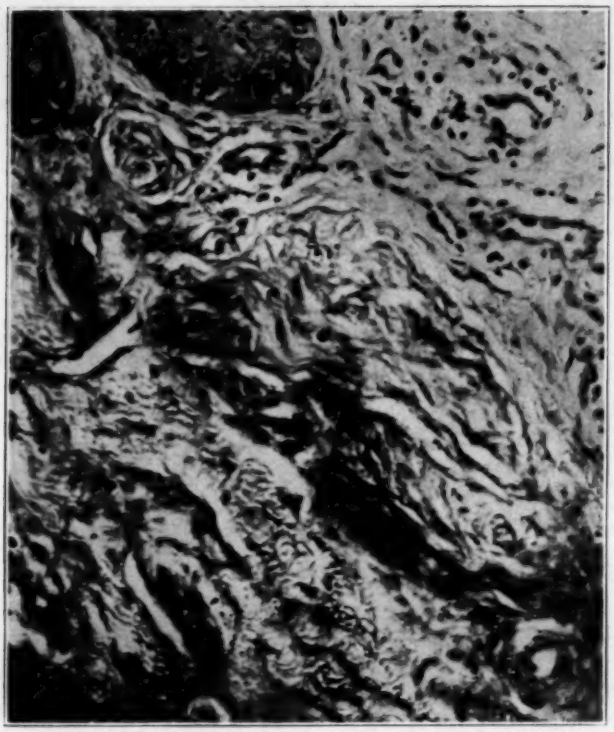

Fig. 6.—Early nerve trunk formation immediately under epiderm.

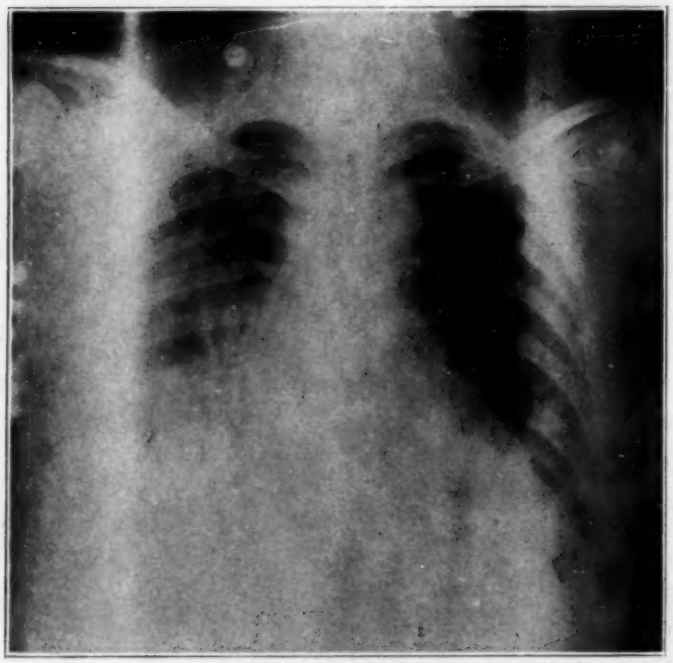

Fig. 7.—Appearance of chest, showing dense opaque shadow in lower portion of right side of the thorax, with costophrenic angle obscured.

considered herself well until four years before she was admitted to the hospital, when the lesions responsible for her admission to the hospital made their appearance.

Physical Examination.—A roentgenogram of the chest showed cottony infiltration of the left apex suggestive of an old inflammatory condition, probably tuberculous in origin. Dense opaque shadows in the lower portion of the right thorax, with the costophrenic angle obscured, suggested a thickened pleura with fluid.

The manifestations on the skin were limited to the extremities, the face, trunk and thighs being entirely free. On each extremity from 15 to 20 deeply pigmented, discrete, firm, flattened tubercles were noted, varying in size from that

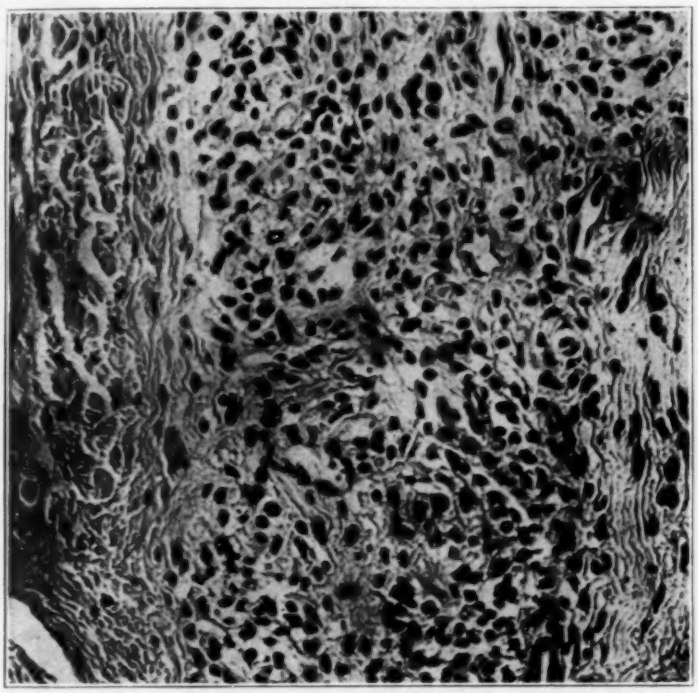

Fig. 8.—Infiltration (fibroblastic and polymorphonuclear) with collagenous tissue at left and newly formed nerves at right.

of a split pea to that of a hazelnut. Several showed an umbilication; they were firmly incorporated in the skin, diffusely distributed and did not follow any nerve trunk.

They began to appear four years before the present examination, new lesions appearing gradually. Except for occasional periods of mild itching, they were symptomless until one year ago when the patient came under observation. At that time she referred to them as having "spells of severe itching," as producing knife-like pain and being both painful and tender on handling, whereas at other times they were neither tender nor painful.

The Pirquet test was positive.

The blood and spinal Wassermann reactions were negative.

A complete blood count showed: red cells, 4,320,000; white cells, 6,200, with hemoglobin, 80 per cent; neutrophils, 57 per cent; lymphocytes, 35 per cent; large mononuclears, 5 per cent; transitionals, 1 per cent, and eosinophils, 2 per cent.

The patient had been given old tuberculin at irregular intervals. Recent roentgen studies showed improvement of the chest; new lesions had not appeared during the last two months, and the patient believed her attacks of paroxysmal pain were less severe and more infrequent.

Microscopic Report.—The stratum corneum, the stratum granulosum and the prickle cell layer were markedly hyperplastic.

The compelling feature of the corium was the presence of numerous ill-defined strands of medullated nerve trunks which extended in all directions through the subpapillary parts, some being parallel to the surface, and others appearing in transverse section. Particularly striking were those strands which extended in a perpendicular direction as far as the tips of the papillae. There were no inflammatory infiltrates actually within the nerve trunks, but there were comparatively

Fig. 9.—Posterior view of arm and forearm showing presence of papules characteristic of tuberculid; cutaneous neuroma.

dense accumulations of lymphocytes around them. The nerve fibers were traceable into the deeper portions of the corium, but there was much less here than in the subpapillary parts. The large round cell infiltrate was also to be found around the blood vessels. It is significant, however, that the densest accumulations occurred around the nerve tissue, and that the nerve elements occurred under those parts of the epiderm that were the most markedly hyperplastic. The nerve distribution was not a peculiarity of the anatomy of the entire skin of the patient. Large numbers of fibroblasts, congregated in the perivascular lymph spaces, might well have been expressions of a diffuse granulomatous infiltration.

Van Gieson's stain distinguished the yellowish-brown involuntary muscle bundles deeper down from the strongly red nerve trunks. The fibrillar portion of the nerve trunk stained pink; the medullary sheath stained yellow.

Ziehl-Neelsen's method did not demonstrate any acid-fast cells.

Neuroma cutis, therefore, would imply a new growth, located intimately within the skin. Frequently these growths assumed the character and distribution of tuberculids, but occasionally they are solitary; they are of various sizes, are commonly tender and painful, and contain abnormal nerve elements.

Thus far the diagnosis has been made only by the microscope. Heidingsfeld comments that "all excessively and persistently painful lesions of the skin, in which the pain is of a spontaneously paroxysmal, or easily induced character, warrant careful technical examinations for nerve fibers."

The essential pathologic process is located in the corium, and consists of a meshwork of nerve fibers—medullated or nonmedullated—supported by a connective tissue stroma. There may or may not be present other elements, such as blood vessels, lymphatics, elastic tissue, unstriated muscle and various cells, indicative of a granulomatous stimulus.

The search for etiologic sequence is concentrated on the abnormal nervous tissue. Are the nerve elements found in these lesions dislocations of normal nerve trunks? The "American Textbook of Pathology" [11] points out that certain tumors "may take their origin

Fig. 10.—View of arm and forearm showing presence of papules characteristic of tuberculid; cutaneous neuroma.

from the endoneurium, pushing aside the nerve fibers until they become widely separated," and that "it should be clear, therefore, why a histological study of the neurofibromas as found in the skin and along the course of peripheral nerves should show gradations relative to the nerve fibers which are sometimes abundant, again isolated, or even absent, and why the fibers vary from apparently normal medullated fibers to naked axis cylinders or axis cylinders variously formed."

Louis Heitzman [14] also questioned "whether the nerve fibers in neuromata cutis are newly formed. If the internal nerve sheath be increased, the innumerable nerve fibers are pushed apart and thus may give the impression of constituting a true neuroma."

In the present case, moreover, it appears as though there may have been a larger nerve trunk, but that it has become split into separate subfasciculi, a dendritic separation and distribution of one of the nerve

14. Heitzman, Louis, in Morrow, P. A.: System of Urology, Syphilology and Dermatology, New York, D. Appleton & Company, 1894.

filaments in the skin. Sufficient evidence seems to be at hand, therefore, to warrant the conclusion that the nerve elements may represent the disintegration of some parent nerve trunk. On the other hand, a distinction should be made between tumors that take their origin from the endoneurium, and nodules, such as tuberculids, that depend on a toxic stimulus producing focal granulomatous reactions. The fibroid and plexiform tumor, the neurofibromas of Recklinghausen, painless embryonic connective tissue and new growths are accredited with

Fig. 11.—Lateral and posterior view of leg showing hazelnut-sized nodules and note scratch marks; cutaneous neuroma.

hereditary characteristics, and with arising from embryonic rests. They are tumors in the exact meaning of the word. The nodules under discussion are the result of acquired irritants, irritants that produce degenerative and proliferative reactions, and pain when contact is made with sensory nerves. Heidingsfeld pertinently remarked:

> The explanation that the pain in myoma cutis is due to mechanical pressure scarcely suffices. Otherwise all growths in the cutis would give rise to similar symptoms.

As is well known, the nerves are nothing more than axis cylinders, that is, the expansile portion of the nerve cell or soma. In the presence of toxins, poisonous and traumatic actions, the nerve is much more active than the central cell. Thus, while the soma and dendrite possess only slight powers of regeneration, reacting rather by internal or structural metamorphosis, the axis cylinders respond to stimuli not only by structural or intraprotoplasmic metamorphoses but also by external transformations.[15]

That proliferation of nerve tissue, as a result of irritant actions, may be of wider scope than is generally recognized is suggested again by Heidingsfeld when he noted the "marked proliferation of erector pilorum in some of the chronic dermatoses, such as pityriasis rubra pilaris, which are attended with persistently creepy and chilly sensations." He commented that such hypertrophies "can readily be considered an effect rather than a cause, and if this be true, no cutaneous abnormality would be more conducive to involuntary muscle proliferation than a neuroma."

It is proper, therefore, to question whether the meshworks of nerve fibers found in neuroma cutis do not represent proliferations of nerve tissue. My impression is that these nerve elements may be found to represent a true proliferation induced by some toxic or traumatic action.

SUMMARY

A case is submitted of painful lesions, clinically diagnosed as tuberculid and demonstrated by microscope to be neuroma cutis.

Painful lesions in which the pain is of paroxysmal type warrant careful technical search for nerve fibers.

A distinction is made between tumors in the strict sense of the word and nodules belonging to the category of granuloma.

I believe that the nerve elements found in neuroma cutis represent proliferation of nerve elements.

ABSTRACT OF DISCUSSION

Dr. Weidman, Philadelphia: I had the privilege both of seeing the patient and of studying the sections, and might as well at once confess that neuroma was the last diagnosis that I should ever have dreamed could have been correct. When I first saw the patient I thought the disorder looked like a lichen obtusus corneus, on account of the scratch marks and other features described. It was when I looked at the sections that the surprise came, when I saw the large number of nerve trunks. A main supporting feature of Dr. Ludy's contention that this is a nerve hyperplasia is the distribution of the nerve trunks high up. Sizeable nerve trunks are normally present deep down, but when a nerve trunk is found above the subpapillary region the nerve trunks have divided and subdivided to a point at which they are narrow indeed, being scarcely visible. When it was seen that

15. Cajal: Regeneration and Degeneration of the Nervous System, vol. 1, p. 1, first sect.

the nerve trunks were distributed even in the papillae it was evident that this was not a mere splitting of the nerve, but a genuine hyperplasia. I think that it is not a true neoplasm but a neuromatoid hyperplasia in the sense that amputation neuromas are.

An interesting feature of the sections was the swollen condition of the fibrous tissue cells around the nerves. Many of the fibroblasts closely approached the appearance of epithelioid cells and made one think it might be a case of leprosy, but stains failed to reveal the leprous organisms.

As I see it, the outstanding interest in this case centers in the possibility of tuberculous products provoking a hyperplasia of the nerve trunks. It could not be demonstrated that the offending organism was tuberculous, but in view of the other (clinical) features it is reasonable to suppose that it was tuberculous at foundation, and that the nerve hyperplasia was sufficient to result in the swellings that were observed clinically.

Dr. W. W. Duemling, Ann Arbor, Mich.: As Dr. Ludy has pointed out, not a single one of the cases of true neuroma was diagnosed clinically. I wish to emphasize this point, and that special stains are usually necessary in order to confirm the diagnosis. In the case which I reported earlier this year that also was true. It was thought at first that the lesion was a keloid. In most of these cases there is usually an associated pathologic tissue. This may be either fibromatous, lymphangiomatous or endotheliomatous.

LIII.—LEUKOPLAKIA AND CANCER OF THE VULVA*

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Gynecologist, Barnard Free Skin and Cancer Hospital
ST. LOUIS

Nine years ago, I presented in the ARCHIVES a review of my experiences with leukoplakic and malignant lesions of the vulval skin. Since that time I have had considerable additional experience and an opportunity to check up on the final outcome—the five year results—in these cases, so that it seems well to present a brief outline of the conclusions of these investigations.

Forty cases of leukoplakia and 76 cases of cancer of the vulva seen since 1906 are the basis of this study. The material has been available in part through the cooperation of my fellow gynecologists and through the reference of cases by Drs. M. F. Engman, W. H. Mook and Richard S. Weiss. In a large majority of these 116 cases, material was obtained for histologic study through a partial or complete vulvectomy or through biopsy excisions.

LEUKOPLAKIC VULVITIS

First, in regard to the so-called "precancerous" lesions known as leukoplakia or kraurosis, there were in addition to the forty cases of uncomplicated leukoplakia, thirty-nine in which cancer had already developed at the site of the leukoplakia. In the past year there have been two important contributions to this subject, one by Sobre-Casas and Carranza (thirty-seven cases) and one by Graves and Smith (fifteen cases). The latter writers have again raised the question of the use of the term "kraurosis," which I prefer to limit to those cases in which there is a complete symmetrical atrophy of labia and prepuce with flattening of the folds. They prefer to accept kraurosis of the vulva as the all-inclusive term following the custom of many writers in the past, especially the German and American writers; but the more I see of this disease, the more convinced I become that it is the leukoplakia and not the shriveling ("Schrumpfung") of the vulval skin that is of the greatest importance. In only twenty-two of the forty cases of uncomplicated vulval leukoplakia was such a shriveling present.

The area involved usually extends symmetrically from the mons veneris to the margins of the anal ring. The most pronounced leuko-

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plakia is usually around the prepuce and the perineum. At times, however, the involvement is over only a portion of this area, either preputiolabial or perineo-anal, and in a third group there is an asymmetrical distribution over one or the other labia. Of the forty cases in my series, there were twenty-eight with generalized symmetrical involvement, six with localized symmetrical and six with localized asymmetrical involvement.

Women as a rule do not seek advice for this disease until it has persisted for some time. For this reason, one sees only a limited number in the early stages. At this time, the skin of the vulva is usually somewhat edematous and flabby. About the vaginal introitus, the labia minora and the vestibulum assume a dusky red, a stage that Jayle termed "kraurosis rouge," but over the prepuce and perineum, even early in the disease, are found patches of leukoplakia that have fissures and excoriations. Gradually these patches of leukoplakia become more extensive and fuse with one another until in many instances the whole vulva becomes parchment-like, with a cracked dry surface. The time required for the development of these changes varies greatly with individual patients. Pruritus, which is usually the first symptom, had persisted for an average of more than five years in twenty-seven cases in the series, in which this had been carefully noted, and in seven women the pruritus had existed for ten or fifteen years before the patients sought aid. Therefore many of them were excessively nervous as a result of the insomnia produced by the intractable itching.

Vulval leukoplakia is essentially a disease of the menopause, the average age of the patients being 49 years. In 75 per cent a cessation of menses had occurred, and in a majority of the remaining 25 per cent some disturbance of ovarian function was noted. In two instances a pregnancy was either coincident with or followed the vulval leukoplakia. In one woman, aged 26, referred by Dr. Engman, the pruritus dated back to the onset of menstruation at 13 years. Although the patient noticed the blanching and thickening of the skin of the vulva for a long time, she did not consult a physician until about a year before I saw her, when she married and found it impossible to have sexual relations. The lesions were of the generalized symmetrical type, and histologic examination of the tissues showed the characteristic lesions of vulval leukoplakia. It is difficult to correlate these cases with the assumption of a deficiency of ovarian secretions. Possibly the explanation lies here in a developmental anomaly localized about the vulval skin and due primarily to alterations of pituitary hormones.

Because of the relative infrequency of both leukoplakia and carcinoma of the vulva, it is not surprising that only rarely does one see the actual transition of the one into the other; yet the history of the pruritus and changes in the skin preceding the development of the

tumor is usually such a definite one that there can be no reasonable doubt of their casual relationship. If during an equal period of years I have seen forty cases of leukoplakic vulvitis without cancer and thirty-nine cases of leukoplakic vulvitis with cancer, I think that it is fair to assume that in approximately 50 per cent of patients with vulval leukoplakia a malignant change will develop. Other writers have given

Fig. 1.—Leukoplakic vulvitis with complete obliteration of labial and preputial folds (kraurosis). The symmetrical distribution involving the perianal skin should be noted.

somewhat higher percentages, but even this conservative figure of 50 per cent makes one realize the importance of this lesion as a "precancerous" condition. While there may be considerable periods of time in which the vulval leukoplakia remains stationary or even shows a slight tendency to diminish, I have failed to observe any actual spontaneous or nonsurgical cure extending over five years. Furthermore,

the average age of the forty patients without cancer was 49 years, and the average age of the thirty-nine with cancer was 64 years. In other words, as the disease continues and the woman becomes older, the tendency to a malignant change increases.

TREATMENT

Endocrine treatment, in the form of either hypodermic injections of ovarian, lutein or pituitary extracts, or a stimulating dose (400 milligram hours) of radium applied vaginally to influence the ovaries in younger persons, has failed to produce any appreciable result; so, also, has irradiation of the leukoplakic skin with the x-rays or radium. When a vaginal discharge was an exacerbating factor in the pruritus, douches, taken regularly, gave temporary improvement, but in no cases was a cure effected by any of these measures. At the present, the sole standby is operation, and since the final results of vulvectomy in these cases is so satisfactory and the operation is not dangerous, there should ordinarily be no need for hesitancy in recommending this procedure. If only twenty-five of my forty patients were subjected to vulvectomy, this was due in part to the refusal of some of the older patients to submit to any surgical procedures.

Those interested in the technic of such a vulvectomy will find it described elsewhere.[1] Suffice it to say here that it is important to remove all the involved skin from the mons veneris down to and even sometimes including the perianal skin. If the vulvectomy is partial, there is apt to be a recurrence requiring subsequent operations. On the other hand, I found that of seventeen cases in which a complete vulvectomy was done and a careful follow-up was obtained, in sixteen permanent cures were effected and in nine of these the operation had been performed more than five years previously. In other words, operative measures are almost 95 per cent satisfactory. In two instances a small spot of keratosis less than 1 cm. in diameter, noted at the edge of the operative area several years later, was successfully removed by simple cauterization and did not return.

MICROSCOPIC CHANGES

Material was obtained from a total of sixty-four cases of leukoplakic vulvitis, in thirty-nine of which the condition was carcinomatous. Blocks of tissue were taken from different areas free from malignant changes. Occasionally there was found variation in the character of the lesions in the same patient, but in the main the histologic picture corresponds with the course of the disease.

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1. Nelson's Loose-Leaf Living Surgery, New York, Thomas Nelson & Sons, 1928, vol. 7, chapt. 32.

Berkeley and Bonney have described four stages of this disease, but it seems to me better to limit the description to two, first the hyperplastic, and second the atrophic, stage.

In the early stage, one finds extensive subepithelial leukocytic infiltration with pronounced elongation of the epithelial papillae (acanthosis) and beginning thickening of the keratin layer. In the beginning, nuclear elements are still present to some degree in this keratin layer, and the term parakeratosis has been applied to this stage to distinguish it from the later hyperkeratosis in which only thickly packed

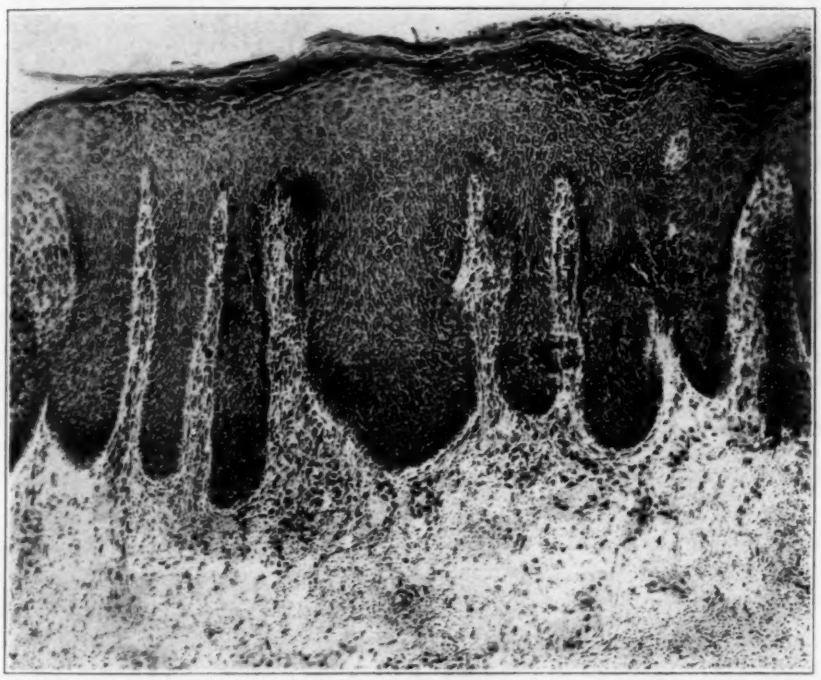

Fig. 2.—Leukoplakic vulvitis: early hyperplastic stage. The keratosis, increased eleidin layer, marked acanthosis and round cell infiltration in the papillae of the dermis should be noted.

keratin fibers are found. In the course of a few months or a year, if the pruritus has been pronounced, there is noted a marked increase in the thickness of the eleidin layer and in the quantity of eleidin deposited in these cells. Since this substance stains deeply with hematoxylin, this layer often appears as a thick black band beneath the keratin. The epithelial layer in this early hyperplastic stage is as a rule from four to six times thicker than that in the normal patient. In the connective tissue, there is considerable hyperemia and marked round cell infiltration. Only toward the conclusion of this stage does one notice increasing tissue formation with some sclerosis.

The late atrophic stage is not an abrupt change. There are gradations between it and the hyperplastic stage, so that areas midway between the two are commonly found. Yet the lesions of this stage are so characteristic and different from those in the early stage that histologically, it seems, almost like two diseases. As the late stage approaches, one observes increasing hyperkeratosis, pronounced eleidin but lessened acanthosis. The papillae become much flatter and shorter even though the total thickness of the epithelial layer is still twice that of the normal. There is also diminished round cell infiltration and increasing sclerosis of the dermis.

The typical late atrophic stage presents a distinctive picture. It is the one described by Breisky and is found almost invariably in those cases showing obliterated labial and preputial folds (kraurosis). The epithelial layer in these cases consists of a considerable layer of hyperkeratosis, beneath which is found a thin layer of eleidin cells and then, with papillae absent, a flat strip of pavement cells that may or may not be covered by a single layer of basement epithelium. In many areas the border of this pavement epithelium appears frayed out and irregular, without any sharp distinction from the connective tissue beneath. Even more marked are the changes in the dermis. The round cell infiltration is in more or less circumscribed lymph zones, much less marked than in the early stages, with plentiful plasma and mast cells scattered through the connective tissue. In many areas directly beneath the epithelial layer this connective tissue undergoes a peculiar collagenous change, so that the upper part of the dermis has a glairy appearance and contains only a few normal cells.

I have left to the last a description of the elastic tissue in this disease since it has rightly been emphasized by all writers as of great significance. Even in the earliest lesions examined (several private patients had been observed for years before the first appearance of the disease), I never failed to note some diminution in the amount of the elastic tissue between the epithelial papillae of the skin and directly beneath the basement membrane. This absence of elastic fibers became increasingly marked as the disease advanced and was most pronounced in the late atrophic stage of the disease. There was complete absence of these fibers in the upper dermal zone, but directly beneath this area they were piled up like kindling wood in irregular pieces and strips, so that one had the impression not so much of absent, as rather of dislodged, disintegrated, elastic fibers.

A study of the thirty-nine cases in which carcinoma was implanted on a leukoplakic base revealed histologically that in 60 per cent the malignant changes took place in an early hyperplastic area and in 40 per cent in a late atrophic area. Hence, carcinoma may develop at

either stage of the disease, although it is a little more prone to spring from the hyperplastic lesions.

If from the foregoing facts an attempt is made to summarize the development of the disease, it seems fair to assume that the underlying

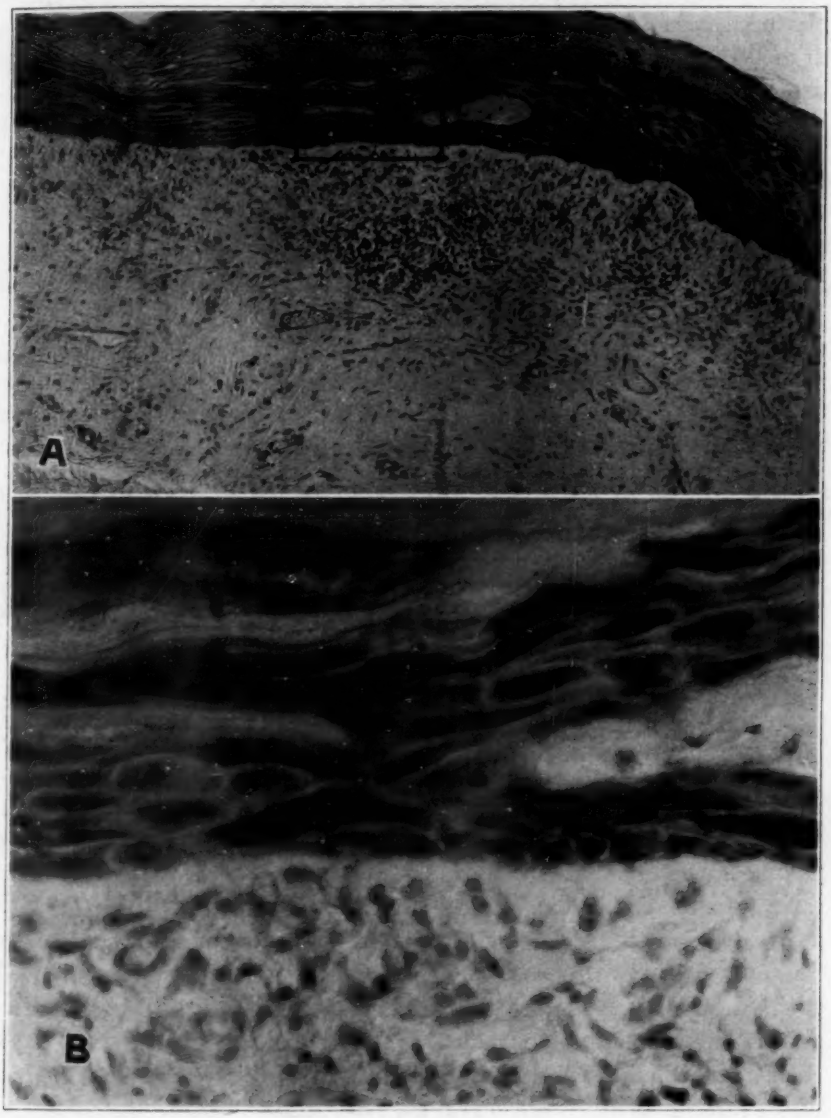

Fig. 3.—*A*, section through skin with beginning atrophy in leukoplakic vulvitis, hyperkeratosis and marked deposit of eleidin throughout the thinned out zona granulosa. Round cell infiltration and sclerosis of the dermis. *B*, area outlined at *A*; high power magnification.

factor is some disturbance of internal secretions (pituitary or ovarian) which brings about an atrophy of the vulvar skin, especially affecting the subepithelial elastic tissue. As a result of this, the skin becomes extremely brittle and through superficial fissures a low grade infection of the cutis takes place. The feeling of rawness or burning that is thus produced is soon superseded by an intense pruritus as the nerve endings in the skin become irritated by the infection. The presence of a vaginal or cervical discharge will greatly hasten the development of these symptoms, and, vice versa, measures taken to correct the discharge and keep the vulva free from infection will retard the symptoms. On the whole, however, the disease makes slow but sure progress and one gradually notes the defense reaction of the tissues in the form of hyperkeratosis and hyperacanthosis. The increased deposit of eleidin in the granular zone of the epithelium is probably also a reaction due to the continued scratching and rubbing of the skin. As the areas of round cell infiltration undergo resolution, the connective tissue of the dermis becomes more sclerotic and undergoes a peculiar collagenous degenerative change. The epithelial layer loses in vitality, the papillae shorten and become obliterated and there is finally left only a thin layer of cells with a coating of old keratinized epithelium. The basement membrane loses its integrity at a relatively early stage and permits an outgrowth of epithelial elements downward. In the later stages, the basal layer of epithelium assumes an irregular, frayed out appearance. Thus, conditions are present which in otherwise susceptible persons lead to the development of a carcinoma.

CARCINOMA OF THE VULVA

I shall pass more briefly over the analysis of the seventy-six cases of carcinoma of the vulva, since they present fewer matters of interest for the dermatologist. The average age of these patients was 59, just ten years older than the average age of the leukoplakic patients. The youngest patient was 26 and the oldest, 87. Of special interest was the rarity of this disease among negresses. Although the clinics were in a negro district, only three of the seventy-six women in my series were colored. This corresponds to the relative rarity of cancer of the skin in the negro race. The greater elasticity of the vulval skin in the negro and the presence of pigment are probably important factors. In this connection, it is interesting that the only leukoplakic vulvitis in a negress that I have seen developed on an area of vulval leukoderma.

There are four distinct anatomic types in cancer of the vulva: (1) cancer of Bartholin's gland; (2) cancer of the glans of the clitoris; (3) epidermal cancer; (4) vestibular cancer.

Cancer of Bartholin's gland and cancer of the glans of the clitoris are essentially subdermal in their origin and development. They are rare and usually malignant. The epidermal and vestibular cancers are of special interest. The former usually originates from an area of leukoplakia. Occasionally, they spring from warts, and in other instances the etiology is not clear. This epidermal type, however, is relatively frequent and relatively benign. The point of origin is most often the labia or the prepuce. It is important not to classify the preputial cancers as cancers of the clitoris. Clinically and histologically, they are quite different. The preputial cancer has all the aspects of

Fig. 4.—Carcinoma of labia on a leukoplakic basis, showing superficial involvement.

cancer of the skin (pearls, pavement epithelium, etc.), whereas cancer of the glans of the clitoris has an almost sarcoma-like structure. Of sixty-nine cases in which a diagnosis of point of origin could be made, there were fifty-one cases of the epidermal type.

Next in frequency was the vestibular type, of which there were ten cases. Here the points of origin were the periurethral tissues or the fourchet. Both clinically and histologically, cancers of this type were more malignant. The point of greatest interest, however, was that in eight of the ten cases a close relationship was established between the cancer and a previously existing tertiary syphilitic ulcer, so that

it can fairly be said that in this type syphilis is usually the etiologic factor. It is also to be noted that whereas the average age of the patients with leukoplakic cancer was 64 years, the average age of these eight syphilitic patients with cancer was 38 years. In other words, one must distinguish in women before the menopause a very malignant type of cancer on a syphilitic basis, which springs from the vestibular portion of the vulva.

Fig. 5.—Carcinoma of prepuce, everting type, associated with leukoplakia of surrounding vulval skin.

The symptoms of cancer of the vulva consist primarily of pruritus, burning on urination and the development of an ulcer that persists and causes slight bleeding at times. Since the ulcer is not vascular, the bleeding is at times absent. In any ulcer or lump on a leukoplakic basis or any friable papillary growth at the edge of a syphilitic ulcer, one must suspect cancer. In doubtful cases a biopsy should always be made.

An analysis of the various tumors to determine their index of malignancy according to Broders' classification revealed a close relationship between the clinical extent of the disease and the histologic picture. Of fifty-eight cases available for this study, there were seven cases of type I, thirty cases of type II, sixteen of type III [2] and five cases of type IV. This shows that a majority of the tumors are relatively benign.

The best treatment for cancer of the vulva consists of radical surgical removal of the tumor and its tributary lymph glands. The fact that glandular metastases to the femoral and inguinal regions on both sides

Fig. 6.—Carcinoma of glans of clitoris. No leukoplakia or kraurosis. Subdermal tumor.

occur relatively early in the disease has made such a removal of lymph glands seem, *a priori,* the correct therapeutic procedure. The immediate operative results have been satisfactory, but heretofore there have been few reports of five year results, on which alone the value of any therapeutic measure in cancer must be based. In this country, there has heretofore been no attempt to evaluate the methods of treatment for cancer of the vulva, and while the present report of forty-nine cases observed for more than five years is too small to justify positive con-

2. Taussig, F. J.: Leucoplakic Vulvitis and Cancer of the Vulva, Am. J. Obst. & Gynec. **18**:472 (Oct.) 1929.

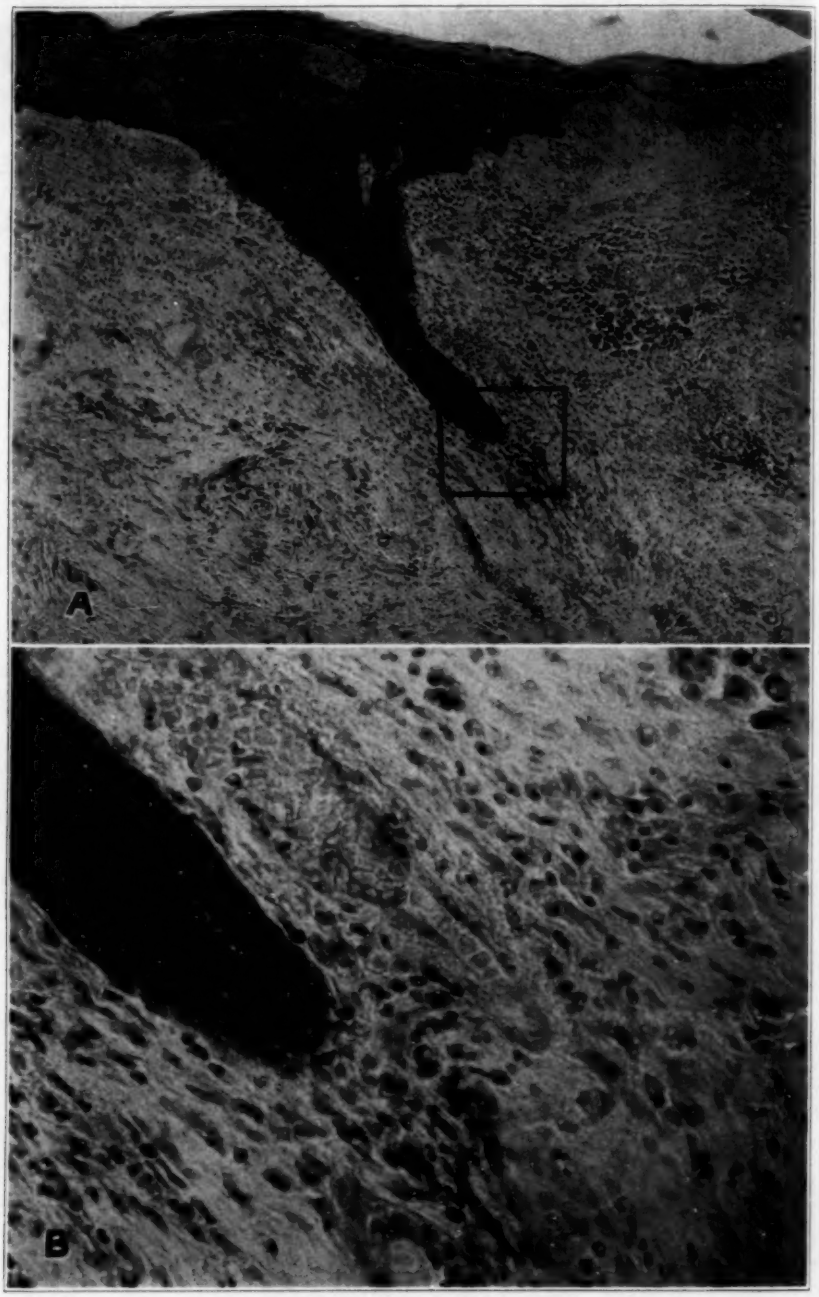

Fig. 7.—*A*, carcinoma at edge of a hyperplastic area of leukoplakic vulvitis. *B*, area outlined at *A*; high power magnification.

clusions, it at least offers a basis for future confirmation or denial. The accompanying table gives a summary of the results. It will be noted that the cases in which operation was performed have been divided into three groups: (1) those in which a simple vulvectomy was done without removal of lymph glands; (2) those in which the vulvectomy was accompanied by the ordinary operation for removal of inguinal and femoral lymphatics, and (3) those in which the vulvectomy was accompanied by the more radical removal of the tributary lymph glands according to Basset's technic. It is characteristic of Basset's method that the deeply situated glands in the iliac fossa to either side of the external iliac vessels are included. These glands can be approached

Analysis of Cases of Vulvar Cancer Observed for Five Years

	Total Cases	Operative Deaths	Died Within One Year	Died Between 1 and 5 Years	Died After Five Years	Died of Other Causes Within Five Years	Cured for Five Years or More	Not Traced	Percentage of 5 Year Cures and Absolute Cures
Palliative or refused treatment	4	..	1	1	..	..	0	2	0
X-ray or radium	15	..	11	2	..	..	0	2	0
Simple vulvectomy	6	1	3	..	..	..	..	2	0
Vulvectomy with superficial or incomplete removal of gland	13	1	3	3	1	1 (4 years later)	4	1	30.7 (5 year) 23 (absolute)
Vulvectomy with complete double-sided Basset operation	11	0	1	1	2	..	9	0	81.8 (5 year) 63 6 (absolute)
Total cases	49	2	19	7	3	1	13	7	26.5 (5 year) 20.4 (absolute)

on the one side by opening the inguinal canal in its entirety and on the other by cutting Poupart's ligament over the femoral ring. Only in this way can these important glands be satisfactorily removed. An analysis of the results shows clearly how important it is to effect such a complete removal, for of eleven patients operated on by Basset's method more than five years ago, nine remained free from recurrence for longer than five years and seven are still alive and free from recurrence at the present time. The immediate operative mortality is practically nil, for in nineteen cases in which the Basset operation has been done thus far, there has been no fatality. Since many of these women were over 65 years of age, it is not surprising that a certain number died of other causes without recurrence. I have, however, not included any of these cases among the cures. It is of course possible that with

larger numbers the strikingly brilliant results obtained with radical operations will be somewhat reduced. I may have been rather fortunate in my results in this series. Nevertheless, it is sufficiently evident, I believe, that the pessimistic views as to operative results in cancer of the vulva are not justified and that the prognosis in this type of malignant disease is more favorable than in cancer of the cervix or of the ovary.

The results of irradiation with either the x-rays or radium offer a striking contrast, for in my series there were no five year cures, and the frequency of severe and late burns following treatment has so discouraged me that I am willing to abandon this method of treatment except in a few instances in which operation is contraindicated. Since the radical operation of Basset can readily be performed under scopolamine morphine and local anesthesia, the number of operative contraindications is extremely small.

The value of the complete removal of the glands is further emphasized by the histologic study of the glands removed at operation, for even a relatively superficial examination of such glands showed metastases in more than one third of the cases. In two of the nine patients who have remained cured for more than five years, metastases in the lymph glands were found.

CONCLUSIONS

The incidence of cancer of the vulva can be reduced about 50 per cent by timely removal of the "precancerous" lesions, a complete vulvectomy for leukoplakic vulvitis.

The treatment for such a cancer with the x-rays and radium is attended by unsatisfactory end-results. On the other hand, a complete vulvectomy with removal of the tributary lymph glands by Basset's technic gives brilliant immediate and final results after five years. A permanent cure can reasonably be expected in two of every three cases.

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References previous to 1920 will be found in Graves and Smith, Labhardt and Taussig (Diseases of the Vulva).

LATE SYPHILIS OF THE PALATE

A HITHERTO UNDESCRIBED FORM OF PALATAL SYPHILIS*

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In the last ten years I have several times seen patients with a form of palatal syphilis such as is herein described, although the condition was not nearly as well marked as in the present instance.

REPORT OF A CASE

A very light-colored mulatto man, aged 40, was referred on Dec. 10, 1928, to the clinic of Dr. J. Frank Schamberg for treatment of latent (?) syphilis that had been discovered accidentally by routine complement-fixation (Kolmer) and precipitation (Kahn) tests, both of which gave strongly positive reactions.

Fig. 1.—Sclerous palatal mucositis.

On physicial examination, the only abnormality found was the oral condition. On the palate (fig. 1), extending from its anterior third back over the posterior two-thirds and part of the soft palate, was a well marked, irregularly elevated plaque (possibly from 4 to 5 mm. at its thickest point) composed of firm, grooved, rather closely placed convolutions. The mucosal surface was smooth, intact and of a grayish leukokeratotic appearance. There were no subjective symptoms, and the patient was unaware of its presence until I called his attention to it.

A section was removed for histologic study. It showed, in addition to a granular and keratinized layer, mild acanthosis and papillomatosis, a marked round cell infiltration and a definite increase in fibrous tissue (fig. 2).

A mixed treatment of neoarsphenamine, 0.45 Gm. and potassium bismuth tartrate, 0.1 Gm. was given once a week. By the sixth treatment, there had been fully 75 per cent regression in the size of the plaque (fig. 3). When the patient

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Fig. 2.—Fibrotic changes in the derm and the cellular infiltrate plus the keratosis, granulosis and acanthosis are clearly visible.

Fig. 3.—Same patient as in figure 1, after treatment.

was reexamined on July 10, 1929, the palate had become normal except for the surface which still had a slight leukokeratotic appearance. He had continued smoking during the entire period of treatment.

COMMENT

For this form of syphilis, I propose the term sclerous palatal mucositis.

The usual form of chronic syphilis of the palate, the gumma, with or without rupture or perforation into the nose is well known. The special clinical appearance of the lesion shown in figure 1, its firmness, indicating that it had been present for some time, would tend to exclude the simple gumma, as would the fibrous changes found histologically. However, it may be considered a form of diffuse gummatous infiltration with a tendency to fibrosis. It must not be confused with simple leukoplakia, which would have been uninfluenced by antisyphilitic treatment alone, nor with the anomaly taurus palatinus in which the surface is smooth but not grooved and which is congenital; nor must it be confused with the condition, a case of which Howard Fox[1] presented before the New York Dermatological Society as "gray rugae of the hard palate," in which there are rows of narrow, firm, whitish ridges located on the anterior third of the palate and which is likewise a normal condition found in many persons. Mucous adenomas may be confused with sclerous palatal mucositis, but they are isolated lesions and form pinhead or slightly larger-sized rounded, firm elevations.

Sclerous palatal mucositis appears to bear a close relationship to sclerosing glossitis.

1714 Pine Street.

1. Fox, Howard: Gray Rugae of the Hard Palate, Arch. Dermat. & Syph. **19**:139 (Jan.) 1929.

ACUTE VESICULAR ERUPTIONS OF THE HANDS AND FEET *

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Darier [1] stated that "when one is faced with a dyshidrosiform eruption the problem is to decide between either (1) parasitic epidermatophytosic dyshidrosis, or (2) non-parasitic dyshidrosis, or occupational dyshidrosiform dermatitis." Since Mouktar [2] (1892) called attention to the fact that many cases are mycotic, there has been a growing tendency to blame this infection. Recently, Mitchell [3] reported his failure to find fungi in dermatoses that simulate mycotic pictures. He quoted Rajka, who stated that there are three forms of dyshidrosis: mycotic, microbic and nonparasitic, and that it is his belief that further study might lead to the placing of many of the cases of the third group into one or the other of the first two groups. The sudden change exhibited by certain dyshidroses into pyoderma suggests microbic origin in them, although it cannot be definitely determined whether the pyogenic infection is primary or secondary. The failure to find fungi in vesicles of the hands in cases that have dermatophytosis of the feet,[4] and the focal reaction in the vesicles from injections of trichophytin [5] lend support to the theory that some of them are allergic in nature. The dermatitis is also caused by chemical agents, and occasionally accompanies erythema multiforme and eczema on other parts of the body.

After considering the aforementioned causes, one wonders whether the term "dyshidrosis (pompholyx)" may properly be used in any but in an adjectival sense.

Such textbook descriptions as "deep-seated character of the lesions, their symmetrical distribution, and their occurrence in crops" [6] and

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* Submitted for publication, Aug. 27, 1929.

*Read before the Section on Dermatology and Syphilology at the Eightieth Annual Session of the American Medical Association, Portland, Ore., July 12, 1929.

1. Darier, J.: Dyshidrosis: Its Parasitic Nature, Lancet **2**:578 (Sept. 27) 1919.

2. Mouktar, quoted by Darier: Lancet **2**:578 (Sept. 27) 1919.

3. Mitchell, J. H.: Amycotic Dermatoses Simulating Ringworm and Erosio Interdigitale Blastomycotica, Arch. Dermat. & Syph. **19**:659 (April) 1929.

4. Williams, C. M.: The Enlarging Conception of Dermatophytosis, Arch. Dermat. & Syph. **15**:451 (April) 1927.

5. Bloch, B., discussion on Mitchell, J. H.: Arch. Dermat. & Syph. **19**:659 (April) 1929.

6. Sutton, R. L.: Diseases of the Skin, St. Louis, C. V. Mosby Company, 1926, p. 292.

"circumscription of the lesions to the lateral digital and palmar surfaces" [7] are seen to apply equally well to an occupational dermatitis, or to a mycotic dyshidrosis as to a case which for the want of an etiologic diagnosis has to be pigeon-holed into the pompholyx (dyshidrosis) group.

It is common to see such influences as season, age, sex and nervousness which are known to affect "pompholyx" also to apply to the other dyshidrotic eruptions.

A patient with a recurring simple pompholyx is more susceptible to irritation or infection of the hands and feet.

Fig. 1.—Deep-seated vesicles of pompholyx.

Two clinical signs commonly appear sooner or later in a patient who has a recurring dyshidrosis: (1) vesicles along the lateral borders of the digits, (2) the occurrence of a plaque of vesicles in the center of each palm, and at times on the same area of each foot.

I have seen also that constitutional treatment helps all of them regardless of external causative factors.

For the foregoing reasons I believe that internal factors influence all vesicular eruptions of the hands and feet. The problem, therefore, is analogous to the explanation of eczema: (1) the term is generic and (2) the causative factors may work in various combinations.

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7. Schamberg, J. F.: Diseases of the Skin, Philadelphia, W. B. Saunders Company, 1908, p. 91.

In hot climates these eruptions create a problem. They are common. Recrudescences vex both patient and physician. And it is difficult to get a speedy recovery of the cases complicated with a severe pyoderma.

I collected the cases of all patients seen in 1928 who presented vesicular eruptions only of the hands and feet, with the object of studying the relationship existing between them and various internal disturbances. I have been led to believe that the state of the skin, influenced by the body as a whole, is an important determining factor for the outbreak of the eruption. In other words, the governing influences which have been ascribed to pompholyx underlie all dyshidrosiform eruptions. If such is not the case, how else can the following questions be answered?

Fig. 2.—Vesicles along the lateral surfaces of the digits.

QUESTIONS

1. Why is it that fungus infection causes a vesicular eruption that is confined only to the hands and feet? Why are not other areas of the skin affected in that particular person? What explains a dermatophytosis producing a vesicular dermatitis in certain persons and not in others, or in the same patient at different times?

2. If an external irritant explains a case, why are not other regions involved where the skin is certainly more sensitive?

3. What is the explanation of the symmetry of the eruption?

The last question points more forcibly than any to the fact that internal factors are at play.

The cases were divided according to table 1. In the pompholyx group were placed those cases which fitted the clinical picture of the condition, or in which no causative external factor was incriminated or even suggested. It is seen from table 2 that these dyshidrosiform eruptions have occurred more prevalently during the hot season and have affected persons below the age of 40 (those most active) more than those above this age. The greatest difference according to sex has occurred in dermatophytosis. Pompholyx occurred in more females

TABLE 1.—*Areas Involved in Each Condition*

Diagnosis	Number of Cases	Of Feet	Of Hands	Of Hands and Feet
Dermatophytosis	86	60	4	22
Dermatitis venenata	25	4	20	1
Pompholyx	20	0	17	3
	131	64	41	26

TABLE 2.—*Incidence of Vesicular Eruptions According to Season, Age and Sex*

	Seasonal Incidence											
	Jan.	Feb.	March	April	May	June	July	Aug.	Sept.	Oct.	Nov.	Dec.
Dermatophytosis	(Vesicular type occurs uniformly throughout the hot season which is from May to November)											
Dermatitis venenata	1	1	2	1	3	2	1	2	2	8	2	0
Pompholyx	0	0	1	1	3	0	1	5	4	4	1	0

	Age		
	17-30	30-40	Over 40
Dermatophytosis	19	54	13
Dermatitis venenata	5	18	2
Pompholyx	8	6	6

	Sex	
	Male	Female
Dermatophytosis	52	34
Dermatitis venenata	14	11
Pompholyx	7	13

than males, but the number of cases is too small to be absolutely conclusive.

REPORT OF CASES

The following cases were selected to point out the various internal disturbances that have been seen commonly associated with vesicular eruptions of the hands and feet.

Classic Pompholyx.—CASE 1.—Mrs. R. C. T., aged 45, was seen with a pyoderma of the hands which started as a vesicular eruption. She had dyshidrosis in hot weather regularly for the past fourteen years. No external agent was accountable, nor was there anything in the general health to be blamed.

Toxic Absorption.—CASE 2.—Pete M., a boy, aged 17, was seen with cellulitis which began as pyogenic infection in the web of a toe, and which was irritated with iodine. Deep-seated, painful vesicles and bullae then appeared over

the plantar surfaces. Pustulation quickly ensued. Three days after the onset of the acute dyshidrotic eruption of the feet the palmar surfaces became affected similarly. No other areas of the body were affected. He had never had any symptoms or signs of dermatophytosis.

CASE 3.—Mrs. Cl., aged 34, was seen on Oct. 5, 1928, with an acute vesicular dermatitis uniformly covering the palmar surfaces of the fingers and hands in a symmetrical manner. Tremor of the fingers was marked. The eruption appeared the day after an abscessed tooth was extracted. After the skin became normal, another tooth was extracted, and the dyshidrosis reappeared. Was the cause toxemia from the tooth or from the procaine hydrochloride?

Diet.—CASE 4.—Dr. B., a man, an internist, stated that he could produce a pruritic dyshidrosis of his fingers, chiefly of the index finger, by overingestion of sweets.

CASE 5.—W. S. K., a middle-aged man, was seen with symmetrical arrangement of vesicles and bullae over the palmar and plantar surfaces. Being a native

Fig. 3.—Tinea unguum and mycotic dyshidrosis.

of the north, he rarely partook of Mexican dishes, for which he had a craving. For the previous three days he had eaten heavily of this highly seasoned food. This plus the extremely hot weather at the time were the only explanations for the eruption, which was his first attack.

CASE 6.—S. M. F., a man, aged 26, a very nervous clothing salesman, presented a vesicular eruption symmetrically distributed over the palmar surfaces of the fingers and palms. He drank from ten to twelve cups of coffee daily.

Nervousness, Chief Symptom.—CASE 7.—Mrs. S., aged 35, had a vesicular eruption of the fingers and toes that had recurred for three months. Fungus infection was not demonstrated. She had numerous bad teeth and pyorrhea, complained of indigestion and constipation and was very nervous. Tremor of the fingers was marked.

CASE 8.—In W. C. F., a man, aged 38, a vesicular eruption first appeared along the lateral borders of the fingers, and later involved the palmar surfaces, during the previous three weeks. Two weeks before, vesicles were present on the insteps and along the feet. His physician discovered a secondary anemia, and

said that he was of a highly nervous temperament. Tremor of the fingers was marked. I observed him from Sept. 10, 1928, to Nov. 30, 1928, when his hands became normal, during which time he continued his pressing duties as manager of a retail store. He returned on Jan. 3, 1929, and said that as soon as he began having toxic symptoms from a recent acute respiratory infection, the "blisters" reappeared on his fingers.

CASE 9.—E. C., a girl, aged 18, had dyshidrosis which appeared on the lateral borders of the fingers ten days before each period. The condition was worse in hot weather. A fine tremor of the fingers was present.

Fig. 4.—Bilateral dyshidrosis in the center of each palm. No fungi were found in the hand. The patient had dermatophytosis of the feet.

Dissipation.—CASE 10.—W. A. B., a man, aged 41, said that a vesicular eruption had occurred on the lateral surfaces of his fingers in hot weather for the past three years. There was tremor of the fingers. He complained of frequent indigestion. He smoked from ten to twelve cigars daily. He drank heavily and often, and was under nerve tension constantly from his business.

Dissipation and Fungus Infection.—CASE 11.—Dr. G., a man, aged 58, was first seen in August, 1924, with a vesiculopustular eruption and cellulitis involving uniformly and symmetrically the palms and soles. The eruption had incapacitated him in the late summers of 1924, 1925 and 1926 for about a month. Fungus was

easily demonstrated. It had been definitely proved that over-use of alcohol aggravated the eruption. In 1927 and 1928, he was a teetotaler, and whereas a mild dyshidrosis appeared, he was not bothered as he was during the previous years. Another important influence together with the alcohol was worry over marital difficulties.

Eczema That Appeared First as Pompholyx.—CASE 12.—Miss B., aged 40, had been seen at various intervals annually since 1922. The dermatitis began as pompholyx, but had appeared for several years as plaques of eczema that involved commonly the center of the palms, the hypothenar eminences, one or more fingers and the sides of the ankles. During some stage of its course the individual lesion

Fig. 5.—Cresol dermatitis. (The intracutaneous vesicles and uniform involvement of the dorsal surface are characteristic of external irritation.)

appeared as a fungus infection (similar to Mitchell's [3] cases), yet repeated attempts to culture had failed. The plaques eventually healed, but recurrences were common, and usually reappeared at the old sites. Occasionally, an acute attack was attended with a painful, localized cellulitis, and she had been seen with lymphangitis of the forearm. She had a history of having had a cholecystotomy fifteen years previously. In 1922, she was thoroughly examined and treated by an internist. Drugs internally and outside irritants had been incriminated as causative, and all were disproved. On vacation she did not improve. She was nervous (had marked tremor of the fingers) and was overworked in a responsible position. In March, 1929, the basal metabolic rate was plus 11, and a gastric analysis revealed free

hydrochloric acid 12, and combined acidity 32. Empirically, she was given dilute hydrochloric acid at meal times. The skin healed in a few days. Following an acute rhinitis an acute exacerbation appeared in the same areas which had been affected the previous August. These healed as she recovered her status quo. Recrudescences were better controlled as long as she took the hydrochloric acid.

Case 13.—Mrs. L., aged 41, seen at different intervals between 1923 and 1928, had a dermatitis similar to that in case 11. In January, 1929, she developed an erythema over the trunk, with a weeping flexural dermatitis of the arms, breast folds, over the face and behind the ears, during an exacerbation of the eczema of the hands. She was referred to a clinic for general study. The diagnosis returned was: anacidity and cholecystitis. She had remained on hydrochloric acid since then. There was immediate improvement in the skin condition, and in answer to

Fig. 6.—Dyshidrosis occurred at the recovery from dermatitis exfoliativa arsenicalis. The patient was weak and nervous.

a questionnaire one year later, she said that the dermatitis of the hands was practically nil.

In this connection I would quote Martin,[8] who in an autobiography of eczema manuum (which started as pompholyx) stated that "as regards the cause of my recurrence after eight years' immunity, I can only attribute it to a period of great mental stress and anxiety-illness in my family and business worries—combined with an injudicious use of antiseptics."

8. Martin, H. C.: Eczema: The Psychological Factor in Its Causation, Med. J. S. Africa **21**:155 (Jan.) 1926.

THERAPY

A certain similarity exists in the response of these eruptions to treatment. In combating recurrences and recrudescences, especially in cases that respond slowly to only external therapy (as roentgen and topical applications) attention is directed to general therapy, such as tonics and the establishment of a regimen that will promote normal functions. It is apparent that a microbic or mycotic infection or a chemical dermatitis should receive the logical treatment. In the general care of every patient presenting vesicular eruption of the hands and feet that is of serious moment I use calcium therapy, and I believe that it is of

Fig. 7.—Dyshidrosis with widespread erythema multiforme. Third attack.

distinct aid. It is administered in the form of calcium lactate, thyroid and parathyroid extracts. It has been seen that the tremor disappears, as does the clammy appearance of the skin often enough to be noted, and recurrences are better controlled by its use. Since oral administration is more practical, it has been adopted; however, there is dispute regarding its efficacy.

No calcium estimations of the blood serum have been made. Regarding this point, Loew [9] (who maintained that it is an unreliable index) stated that "it has been commonly observed that, in various diseases

9. Loew, Oscar: The Promotion of Calcium Retention, Brit. M. J. **1**:894 (May 26) 1928.

which readily respond to calcium therapy, the blood calcium was normal, or higher than normal, and not lower, as one would expect." Also, "since the transfer of calcium takes place through the blood, an increase of calcium may be observed in spite of a deficiency of calcium in certain other organs."

The study of calcium absorption particularly concerns the pediatrician, and workers in that field are actively interested in the subject. Holt, Courtney and Fales [10] have shown that there is a variation in cal-

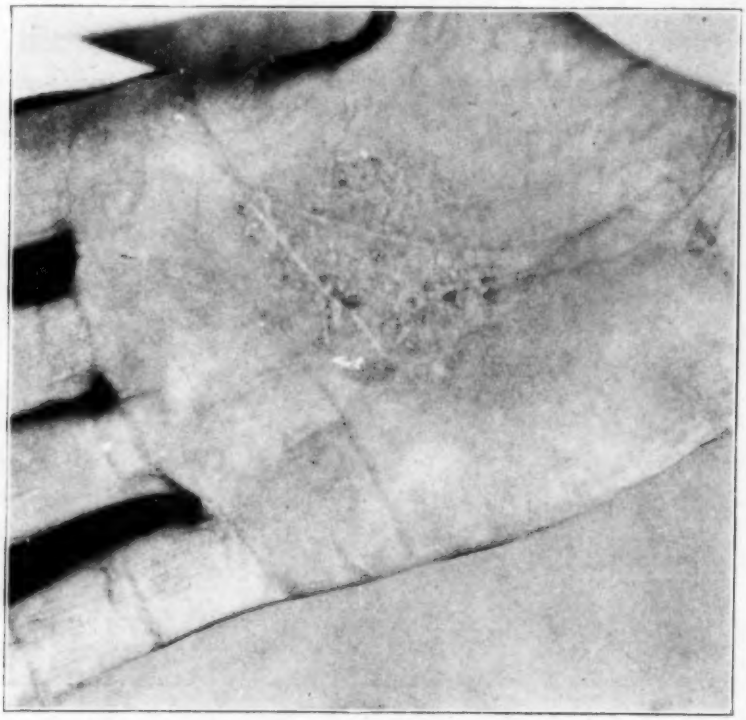

Fig. 8.—The center of the palms and the sides of the digits are common sites for recurrences of any type of dyshidrosis.

cium absorption due to variations of fat consumption. Flood,[11] in a comparison of normal and rachitic infants fed on hydrochloric acid milk, stated that "hydrochloric acid milk increases the retention of calcium chloride in the rachitic infant, but has no effect on the calcium metabolism of the normal baby." This is particularly interesting to me

10. Holt, Courtney and Fales, quoted by Flood: Am. J. Dis. Child. **32**:550 (Oct.) 1926.

11. Flood, R. G.: Calcium Balance with Hydrochloric Acid Milk, Am. J. Dis. Child. **32**:550 (Oct.) 1926.

since two of the cases (associated with eczema) were found to have hypochlorhydria and the eruption cleared with the use of hydrochloric acid.

COMMENT

There are certain clinical signs commonly seen in all dyshidrosiform eruptions: (1) a few have hyperhidrosis, or a clammy skin; (2) a fine tremor of the extended fingers is often seen—this tremor is similar to that seen in hyperthyroidism; (3) the patients are usually nervous, under pressure of duty or responsibility, or are debilitated. Because of the common association of the influences of sex, season, age and the clinical signs mentioned, and because of a similarity in the response to general therapy I believe that internal influences are an important factor in predisposing to all vesicular eruptions of the hands and feet. It is my belief that the underlying pathologic changes are trophic in nature, and are governed by the sympathetic nervous system. This is the only pathway through which all of the aforementioned influences pass. Because of the close interplay between the sympathetic nervous system, the endocrine glands and the viscera, and between the higher centers and the vegetative nervous system, any further discussion as to trophic influences would be purely speculative.

ABSTRACT OF DISCUSSION

Dr. Ayres, Jr., Los Angeles: In the vesicular eruptions of the hands and feet it is important that each case be given a microscopic examination for fungi before regarding it as being due to epidermophytosis. I will admit frankly that in many cases I cannot make a diagnosis of epidermophytosis on the clinical appearance alone. Many patients will show the fungi on the feet and not on the hands. Further investigation of these cases has brought out the point that the vesicular eruption will appear on the feet first and within a week or two on the hands, which leads to the belief that the eruption on the hands is a toxic effect from the infection on the feet. It is common to prescribe Whitfield's ointment and fail to tell the patient when to discontinue treatment, resulting in the development of a true eczema from overtreatment, whereas they first had only a fungus infection. As to the term to use, dyshidrosis I think, is all right for the mild types, but I have come to use the term dyshidrotic eczema for the more severe types. These are accompanied by more marked edema, usually of the hands and feet, but frequently extending to the face and neck as an erythematous rash. Emotional influence may have a definite bearing. In many instances these patients have had conflicts in the family, disturbances in business, too much mother-in-law, and so on. Frequently patients will not volunteer this information, but it is surprising how much a careful history will reveal. I feel that patients with acute and subacute eczema have not been treated properly until a careful emotional history is taken. As to sugar, I think that many of these patients over-indulge in sugar, or if they do not over-indulge they cannot tolerate carbohydrates. Approximately one out of six of these patients in whom no fungi can be demonstrated will show a definite abnormality in the dextrose tolerance test. As to hydrochloric acid, I often find an achylia in these cases. The administration of hydrochloric acid in selective cases is of benefit. Alcohol and focal infection should be emphasized as possible

causes. I wish to call attention to the sinuses. I know that many specialists in nose and throat diseases do not pay as much attention to this source of infection as it deserves. A negative roentgenogram or transillumination does not necessarily rule out chronic sinusitis. Many of these cases can be detected only by a roentgenogram taken in a way that will show the thickening of the membranes, and by a careful sinus irrigation; it is not necessary to demonstrate free pus in chronic cases.

As to treatment, it is possible to have a low skin calcium and normal blood calcium content. The calcium does not do much good if given in small doses immediately after meals. It should be given in water, on an empty stomach, preferably 1 drachm or more dissolved in water, at least twice a day.

Dr. Templeton, Oakland, Calif.: At the University of California, working under Dr. Legge one year ago, we examined the feet of 3,000 students matriculating for the freshman year and found that 54 per cent showed evidence of ringworm. I think that some unknown internal factors may have a bearing on the eruptions of ringworm. These students had no special worries, they had no business worries, the weather was very cool and still 1,600 of them had ringworm of the feet. We studied the effect of hygienic and unhygienic gymnasiums. The girls at the University of California have a new gymnasium with sunny, dry clean floors. They are never permitted to put a bare foot on the floor. We examined them at the beginning and at the end of the year and the incidence of ringworm rose only 2 per cent. The boys, on the contrary, have a gymnasium that is a disgrace to the university, a dark, steamy, wet place, and they run around on the floor with bare feet. The incidence among the boys rose 24 per cent during the school year. I think that although there is some internal factor associated with the development of fungi this is of far less importance than infection.

Dr. Scholtz, Los Angeles: I appreciate the courage of Dr. Lehmann's statement that not all cases of dyshidrosis are mycotic in origin and that some of them are systemic. It has become a dermatologic fashion to deny dyshidrosis as a clinical entity, and to regard it merely as a variety of epidermophytosis. I believe that dyshidrosis is a distinct entity but that, through its common association with hyperhidrosis, it offers a favorable soil for a fungus infection. This accounts for the frequent finding of fungi in dyshidrosis-like lesions. A clear-cut case of the acute attack of dyshidrosis is familiar to all, and presents a different clinical morphology and behavior from vesicular tinea. I cannot conceive how a trichophytic infection can spring over-night into hundreds of uniformly sized, deep vesicles which do not itch or break open, involving both hands, in perfect glove-like symmetry. Neither can I conceive how this multitude of mycotic vesicular lesions can disappear over-night, the way they do in acute dyshidrosis, without any local treatment, by absorption and desiccation. I also find that calcium lactate and solution of potassium arsenite are helpful in the prevention of the seasonal attack of dyshidrosis. I also wish to protest against the prevailing over-emphasis of the importance of the bacteriologic diagnosis of epidermophytosis, leading to the neglect and underrating of clinical diagnosis. The desirability of thorough cultural and microscopic examination in every case is obvious and calls for no argumentation. Yet, in daily clinical work this is feasible and possible only in a small minority of cases. The average clinician is thrown on the resources of his clinical diagnostic acumen in handling the case. For this reason the clinical portrayal and clinical differential diagnosis is desirable and necessary. I believe that the clinical diagnosis of mycotic epidermophytosis dermatoses is possible in an overwhelming majority of cases. The familiarity of the general practitioner with the clinical traits of epidermophytosis would go far toward better clinical control of this type of infection.

DR. FOERSTER, Milwaukee: In a paper on ringworm-like eruptions of the hands, Dr. J. H. Mitchell emphasized the fact that many cases of apparent dermatophytosis are primarily bacterial in origin. This point has not been emphasized sufficiently. Another point worthy of discussion is the one recently brought out by Dr. Sulzberger, namely, that many cases of apparent dermatophytosis of the hands, in which microscopic and cultural examinations are persistently negative, are nevertheless dermatophytosis. They are cases in which dermatophytosis of the hands has occurred by a hematogenous dissemination of organisms from a primary infection of the foot. An allergic state is thought to have developed in the skin with the result that the transplanted fungi die quickly. This accounts for the failure to find organisms and the occasional spontaneous clearing up of such lesions, and also for the development of eczematoid eruptions in the allergic soil. The emphasis placed on dyshidrosis in this presentation is well merited in view of the lack of attention given to this disease in recent years.

DR. HOLLANDER, Pittsburgh: Both the essayist and Dr. Ayres stated that internal administration of dilute hydrochloric acid has benefited some of these patients because it was found that they were suffering from hypochlorhydria. Just like many others, in dermatoses the etiology of which is not clear, I have been subjecting my patients to thorough laboratory work, which, of course, includes gastric analysis, and I have found that in a surprisingly large number of cases hypochlorhydria or even achlorhydria was present. As my percentage of low hydrochloric acid observations was so great, I took this matter up with the internists, who called my attention to the fact that fright and nervousness might have a great deal to do with the low readings I was getting, especially in view of the fact that it was their understanding that the gastric contents contained a great deal of mucus. The point that I am trying to bring out is that single examinations of the gastric content mean little and that in many of my cases in which I have obtained a low reading of hydrochloric acid on repeated gastric analysis I found that the hydrochloric acid became normal without the administration of any medication. I wish to caution Dr. Lehmann that he should make several gastric analyses and perhaps he will find that this is not a factor in so many cases.

DR. MICHAEL, Houston, Texas: I wish to go further with the allergic phase of this problem brought out by Dr. Foerster. Yesterday, Dr. Werner Jadassohn told me that he had just finished a study of vesicular eruptions of the hands. In those cases in which there was a demonstrable fungus infection of the feet, the vesicular eruption of the hands had never shown fungi; they were all trichophytids. Since Professor Bloch's visit last year, Dr. Seale and I have been studying our cases of vesicular eruptions of the hands and have been able to demonstrate fungi in some and none in others. Clinically, the nonfungus could not be differentiated from the mycotic ones. It seems to me that the trichophytin test would assist in solving this problem. By this means, the allergic status of the patient would be indicated and the allergic cases separated from the nonallergic ones. These vesicular eruptions are divisible into four classes: fungus infections, dermatophytids, toxic eruptions and those due to external irritants.

DR. WILLIAMS, New York: I am inclined to believe that some of the eruptions on the hands and feet are not caused by ringworm organisms. I say this guardedly for I am not yet sure. So far as our knowledge goes now, most of the cases are produced by ringworm infection, and the burden of proof is on those who attempt to prove that they are not. The question of allergy is of great interest. We have suspected for many years that some of the cases occurring on the hand were due to allergy. We have not yet discovered why some persons respond with scales and some with vesicles. It may be a question of degree. Some have spoken

of allergy on the hands, and I think that this is the explanation of the vesicular eruption on the palms, but I also believe that much of the eruption on the feet is also allergic. I have examined the feet when there was a large amount of eruption, and have found parts that yielded mycelia in large amount, while in the immediate neighborhood were many vesicles, the more careful examination of which showed no mycotic organism. One woman I saw last winter had a severe tricophytosis which interested me greatly. The laboratory at the clinic reported positive results, but I like to verify my own cases and sent her to the office. There I tried to find organisms in the lesions on the feet and failed utterly, although I took scales and fresh vesicles that were just forming. I was about to give up in despair, when the patient told me that I was not looking in the right place, and that if I looked where they did at the hospital I should probably find them. She indicated the region between the toes and I then scraped the wet, denuded area and found the organisms in large quantities. Another point which raises difficulty is getting an accurate history of the previous existence of dermatophytosis. If the eruption on the hands is allergic, there must have been a previous eruption on the feet. If a lesion of this is not obtainable, it may be that the patient had an eruption on the feet or elsewhere. that he or she was not aware of.

Dr. Wise, New York: I wish to report two patients with vesicular eruptions of the hands which unquestionably resulted from the ingestion of oranges. All tests that could exclude the local irritant action of orange juices were carefully carried out. Therefore, there must be a form of pompholyx eruption from the ingestion of certain foods; for example, oranges. There was a time when the diagnosis of pompholyx was much in evidence. Then a Japanese dermatologist described a fungus in 100 unselected cases of vesicular eruption on the hands. The pendulum swung the other way and nearly every vesicular eruption in the palms is now suggested by every dermatologist who is in a position to make microscopic examinations and culture tests, as probably being caused by the ringworm fungus, either directly or indirectly. But those who have practiced for many years will remember that true pompholyx or dyshidrosis is a definite disease. It may occur in a mother and one or two children who are under the same emotional strain on the same day. I believe that I have often treated patients with true pompholyx. I do not agree with the speaker who said that the vesicle containing a ringworm fungus was probably the result of a secondary infection. I think that pompholyx as described by Tilbury Fox is a disease which exhibits vesicles which are free from pathogenic fungi on the palms and the lateral surfaces of the fingers and which may or may not contain various saprophytic organisms inhabiting the skin of the hands.

Dr. Grindon, St. Louis: A. R. Robinson showed that pompholyx is not connected in any way with the sweat apparatus. What we used to call pompholyx before Sabouraud's description of the epidermophyton was often dependent, as Dr. Wise said, on nervous disturbance. I remember an instance of a superintendent of an insane asylum who developed pompholyx soon after a patient threw a plate at him. Some of these patients get well under the administration of 1/60 grain (0.00108 Gm.) of strychnine three times daily.

Dr. Wile, Ann Arbor, Mich.: I wish to supplement what Dr. Wise said, that there is a group of cases which clinically are indistinguishable from ordinary ringworm infection which have nothing to do with fungus disease. Living as I do in the great goiter belt of this country, I see commonly cases of exophthalmic goiter with acute exacerbations of vesicular eruption on the hands. Microscopic

examination of this type of case is invariably negative for fungus. These patients always recover after operation for goiter, suggesting a further neurogenic origin for the disease. In some cases the disease is markedly benefited by arsenic, which I think also points to a neurogenic basis.

DR. LEHMANN, San Antonio, Texas: I have enjoyed this discussion very much. I did not mean to minimize the importance of fungus infection in relation to this disturbance. I am interested in the practical standpoint of the disorder, i. e., in curing the patients, and that is the reason I take the stand I do. I think that our therapy can be markedly improved by attention to the situation as a whole. I do not wish to enter into the debate of the points brought out. They are almost all included in the paper, but I wish to say that so far as I know Dr. Williams is the first man in this country to give us this important bit of advice, "in vesicular eruption of the hands look at the feet," which I think is well worth while.

News and Comment

INTERNATIONAL COMPETITION FOR A PAPER ON SEROLOGIC METHODS FOR THE DIAGNOSIS OF MALIGNANT TUMORS

An international competition, expiring on June 30, 1930, is open for an original, unedited paper, written from a critical and experimental standpoint, on the following subject: "The Value of Serological Methods in the Diagnosis of Malignant Tumors."

The winning paper will be awarded a prize of 15,000 lire. Only one prize will be awarded.

The paper will be judged by a commission of three, appointed by the president of the Italian Anticancer League.

The Commission will submit a report, together with a proposal for the award, to the Central Board of the League, not later than July 31, 1930.

The papers must be typewritten, anonymous and sent in duplicate to the Headquarters of the League (Rome, 33 Via Triboniano presso Piazza Cavour, Sasa del Mutilato) in a closed envelop bearing a motto on the outside. The same motto must be written on another closed envelop containing particulars of the author's name, address, etc. Papers must reach the address given (free of all postage) not later than June 30, 1930, at midday.

The Italian League reserves the right to publish the winning paper for the first time, and in Italian, in its *Bulletin*.

LUSTIG, President.

GALLENGA, Secretary General.

Abstracts from Current Literature

THE PERIOD OF INFECTIVITY AND SERUM PREVENTION OF CHICKENPOX. J. E. GORDON and F. M. MEADER, J. A. M. A. **93**:2013 (Dec. 28) 1929.

The authors summarize their study as follows: preceding the eruption, chickenpox is apparently infectious for only a brief period, probably not more than twenty-four hours. Infectivity during convalescence is less prolonged than commonly considered, does not necessarily coincide with the persistence of crusted lesions, and probably ceases within ten days. Convalescent serum furnishes a high degree of protection if obtained within one month of the appearance of the eruption. Obtained thereafter it is less efficient, and after five months confers protection in only a third of the immunized susceptible patients.

RAGWEED DERMATITIS: WITH SENSITIZATION AND DESENSITIZATION PHENOMENA. MARION B. SULZBERGER and FRED WISE, J. A. M. A. **94**:93 (Jan. 11) 1930.

The authors report a case of ragweed dermatitis in a man who gave completely negative reactions to skin tests by the scratch method. He did not show any urticarial reaction to any of the substances used, but there was a strongly positive reaction to ragweed when applied by contact for twenty-four hours. After several intradermal injections of allergen, the patient's skin no longer gave a positive reaction to contact with ragweed allergen, and the dermatitis had improved.

HYPERTROPHIC TUMOR OF THE SKIN OF THE LEG ARISING IN A CHRONIC VARICOSE ULCER. W. DONALD BEDFORD, Brit. M. J. **2**:1108 (Dec. 14) 1929.

The tumor was a hard, nodular and papillomatous growth, nonmalignant in character. It extended over the lower third of the leg and foot around the whole circumference.

COEXISTENT HERPES ZOSTER AND VARICELLA. J. M. A. LOWSON, Brit. M. J. **2**:1157 (Dec. 21) 1929.

The patient, a man, aged 36, had herpes zoster involving the posterior root ganglia of the last thoracic and first lumbar nerves supplying the left side of the body. In addition there was an extensive generalized eruption of varicella vesicles in varying stages of development.

OCCUPATIONAL DUST. JOHN C. BRIDGE, Brit. M. J. **2**:1143 (Dec. 21) 1929.

The author stresses considerably that portion of his paper which deals with skin diseases due to occupational dusts. The number of cases for which compensation is being paid for dermatitis produced by dust is increasing every year. The dusts which appear to exert the most rapid and severe conditions are the nitro compounds of benzene and its homologues, for example dinitrochlorbenzene and trinitrophenol (picric acid). There is a large incidence of skin cancers among workers in pitch and arsenic dust, and among workers in coal dust. He refers to the excellent work on occupational skin diseases by Prosser White and closes with a plea to medical men, chemists, and engineers to join forces in the task of prevention of occupational skin diseases.

X-Ray Treatment of the Commoner Microbic Diseases of the Skin. J. B. Higgins, Brit. M. J. **2**:1152 (Dec. 21) 1929.

In a short article, the author reviews briefly the history of roentgen therapy, and the effects of x-rays on tissues. The patients in thirty-seven cases of acne were treated by the fractional method of dosage. From three to ten treatments of 0.5 skin unit each were given. The first three consisted of unfiltered rays; the remaining contained a 0.5 mm. of aluminum filter. Of the thirty-seven cases, there was failure in one; indefinite results in four, and cure in the remaining cases. The author states emphatically that the roentgen treatment of acne vulgaris is the method of choice.

Of thirty-six patients with sycosis treated with x-rays, ten received single epilating doses, nine of whom were cured, while the average total duration of treatment was two months. Of the remaining twenty-six, fifteen received half skin doses and six one-third skin doses. No filter was used. The author feels that mild stimulation of the infected beard produces marked improvement in the majority of cases.

Paronychias did not respond well to roentgen therapy, and with furunculosis the author has had no experience. He comments briefly on the effects of Grenz rays and concludes that they will never replace entirely the x-rays as used at the present time.

Favus of the Male Genitalia. J. Goodwin Tomkinson, Brit. M. J. **2**:1194 (Dec. 28) 1929.

A case is reported in which the dermatitis involved the penis and scrotum. There were typical umbilicated yellow scutula in varying stages of development. The scalp was clean, and there was no involvement of the hairy portions of the genitocrural region. A culture showed growths of *Achorion quinckeanum,* a variety found in the cat and mouse.

Rodent Ulcer Due to Trauma. Norman Paul, M. J. Australia **2**:823 (Dec. 7) 1929.

In an effort to determine just what part trauma plays as a causative factor in the production of basal cell epitheliomas, the author undertook a statistical study with this point in mind. Of seventy-five case histories examined, nineteen patients attributed their trouble to trauma of one sort or another. A similar number had also keratoses (solar). The author concludes that a certain proportion are due to trauma and some to the effects of actinic rays, but in the majority no cause can be assigned.

Erythredema Polyneuritis (Pink Disease) Treated by Ultraviolet Radiation. E. W. Frecker, M. J. Australia **2**:887 (Dec. 21) 1929.

After five weeks of exposure to Quartz light, the patient, aged 10 months, was completely recovered. Features of the disease pointing to an involvement of the sympathetic system, were hypotonus, clammy sweating skin and relaxed vessels in the extremities. The therapy was suggested by the view of Pacini that ultraviolet light exerts a tonic effect directly on the superficial ramifications of the sympathetic fibers in the skin.

Rattner, Chicago.

Severe Case of Duhring's Disease with Basophilic Myelocytes in the Blood and Basophilic Polymorphonuclear Leukocytes in the Contents of the Bullae. J. Nicolas, J. Rousset and R. Froment, Bull. Soc. franç. de dermat. et syph. **36**:671 (July) 1929.

The patient, a woman, aged 45, first developed pharyngitis, then urticaria, buccal bullae, and finally a disseminated bullous eruption, which the reporters

felt could be definitely diagnosed as dermatitis herpetiformis. Her general condition was poor. The unusual cells found in the blood and bullous contents were recorded without definite statements as to their significance.

Dyshidrotic and Vesiculopustulous Generalized Erythroderma Due to Neoarsphenamine. J. Nicolas, C. Pétouraud and R. Froment, Bull. Soc. franç. de dermat. et syph. **36**:675 (July) 1929.

Five days after a third injection of neoarsphenamine, the patient developed a mild scarlatiniform eruption, which disappeared promptly but was followed in fifteen days by a severe exfoliative dermatitis. It is unusual to see a banal dermatitis followed by a severe one without further treatment.

Urticaria Pigmentosa of Adults. J. Nicolas and J. Rousset, Bull. Soc. franç. de dermat. et syph. **36**:681 (July) 1929.

The patient was 55 years of age and had the eruption for four years. It was macular in type. There was no evidence of leukemic blood picture as has been reported in other cases. Mast cells were absent, and are not necessary for a diagnosis.

Lupus Vulgaris of the Face, Leg and Foot. J. Gaté and P. Michel, Bull. Soc. franç. de dermat. et syph. **36**:685 (July) 1929.

The interest in this case lay in the dissemination of the disease. On the face the lesions were nodular, on the leg miliary and nodular, while on the feet they were sclerous.

Lupus Erythematosus of the Face and Buccal Mucosa with Onychosis and Neoplasm of the Knee. J. Nicolas and R. Froment, Bull. Soc. franç. de dermat. et syph. **36**:688 (July) 1929.

The patient presented a typical discoid type of lupus erythematosus on the face with markedly inflammatory patches on the buccal surfaces of the cheeks. All the finger-nails were deformed, friable and longitudinally striated. The nail lesions developed simultaneously with those of the face and mouth. Over one knee was an epithelioma which may have begun in the cicatrix of an old lupus erythematosus patch.

Lichen Atrophicus. J. Gaté and P. Michel, Bull. Soc. franç. de dermat. et syph. **36**:690 (July) 1929.

The authors described a case of this disorder in which the lesions were scattered chiefly on the trunk. The lesions were of typical aspect, and there was no evidence of preexisting lichen planus. Biopsy revealed an atrophic epidermis and in the upper cutis homogeneous hyaline degeneration.

Two Cases of Tuberculosis Verrucosa Cutis in Which Patients Were Cured by Radiotherapy. J. Gaté, J. Coste and P. Michel, Bull. Soc. franç. de dermat. et syph. **36**:698 (July) 1929.

Each case was extensive and severe; treatment consisted of a single hyperintensive, unfiltered dose (H. 17-18).

Tertiary Syphilides Developing on a Scar. J. Gaté, G. Massia and P. Michel, Bull. Soc. franç. de dermat. et syph. **36**:706 (July) 1929.

The case presented the unusual feature of localization of gumma on the scar of a burn received during the war. The significance of this localization is not clear.

CUTANEOUS GANGRENE OF THE INGUINAL REGION FOLLOWING SUPPURATIVE ADENITIS. J. NICOLAS, J. LACASSAGNE and R. FROMENT, Bull. Soc. franç. de dermat. et syph. **36**:710 (July) 1929.

The patient had a small penile ulceration followed by inguinal adenitis and this, in turn, by a vast ulceration. This series of events was produced by streptococci, as shown by laboratory studies. Rapid healing occurred under simple antiseptic dressings.

URINARY SULPHATES IN SOME EXFOLIATIVE DERMATOSES. P. BARRAL and J. ROUSSET, Bull. Soc. franç. de dermat. et syph. **36**:712 (July) 1929.

The authors report the results of an examination of the total urinary sulphates in a few cases of exfoliative dermatitis of secondary type. In general, total urinary sulphur was below the normal figure. The relation between the different urinary sulphur series was modified in some instances.

A CASE OF LUPUS VULGARIS OF LONG DURATION IMPROVED BY GOLD THERAPY. J. GATÉ and P. MICHEL, Bull. Soc. franç. de dermat. et syph. **36**:716 (July) 1929.

The authors report the case of an extensive nodulo-ulcerative lupus vulgaris of the face of eighteen years' duration in which striking improvement followed gold injections. Eight injections with a total dosage of 0.4 Gm. were given.

A CASE OF PEMPHIGUS VEGETANS. J. LACASSAGNE, G. SAMAN and R. FROMENT, Bull. Soc. franç. de dermat. et syph. **36**:720 (July) 1929.

The patient presented a disseminated bullous eruption. The erosive surfaces remaining after rupture of the bullae became rapidly vegetative. His general condition was poor: cachexia and edema of the legs were present.

PROBABLE VEGETATIVE FORM OF DUHRING'S DISEASE. J. GATÉ and P. MICHEL. Bull. Soc. franç. de dermat. et syph. **36**:722 (July) 1929.

A man, aged 50, presented a bullous, vegetative dermatosis which had begun in February, 1929. At its onset, the lesions were crusted, resembling impetigo, but bullae soon made their appearance. Through their confluence and rupture large eroded surfaces remained. Vegetative masses were present in the axillae and inguinal folds. His systemic state was good. The mucous membranes were unaffected.

The authors take up the differentiation from pemphigus; always a moot question in borderline cases. In this case, they regarded the freedom of the mucosa, the relatively good general condition, the evolution in crops and the eosinophilia as strongly favoring the diagnosis of Duhring's disease.

PAINFUL SUBCUTANEOUS NODULES CONTAINING OSSEOUS TISSUE ASSOCIATED WITH SYPHILITIC MENINGITIS. J. ROUSSET, Bull. Soc. franç. de dermat. et syph. **36**:727 (July) 1929.

The patient was seen with progressive paralysis of the lower extremities which was of probable neurosyphilitic origin. He also had some subcutaneous nodules which biopsy revealed to be chiefly lipomas with some areas of osseous tissue. The nodules had appeared singly some time after the neurologic symptoms.

MYCOSIS FUNGOIDES DEVELOPING FROM POIKILODERMA. J. GATÉ and P. MICHEL, Bull. Soc. franç. de dermat. et syph. **36**:738 (July) 1929.

The patient had been presented previously with a diagnosis of poikiloderma, which had been present nearly eleven years. In the early part of 1929, obstinate

ulcers and later tumors, proclaiming the evolution of mycosis, developed. Cases of somewhat similar evolution have been described by Civatte and by Gougerot and Blum.

In the present case, biopsies taken before the apparition of the tumor stage showed an indefinite, banal picture. The tumors, however, showed the histologic structure of lymphosarcoma. Despite this observation, the presenters adhered to their clinical diagnosis, since mycosis fungoides has no pathognomonic histologic picture.

MICHAEL, Houston, Texas.

DERMATOLOGIC ABSTRACTS

THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION

EARLY GANGRENE DUE TO OXALIC ACID IMMERSION. M. GROLNICK, New York State J. Med. **29**:1461 (Dec. 1) 1929.

Grolnick relates the case of a painter who had been scrubbing floors with a solution of oxalic acid for two years at infrequent intervals, and for only a short period of time, in the course of his regular painting jobs. However, during the two previous months he had devoted to it as much as twelve or fifteen hours a week. Furthermore, he had never adopted the protection of rubber gloves. On the day before he consulted Grolnick, soon after one of these floor washings, the patient noticed a drawing pain under the nails of the fingers of both hands. Later the fingers became stiff, so that he was able to flex them only with difficulty. During the night the pain became so severe as to cause insomnia. The complaints were more marked in the right hand. The right hand showed a deep cyanosis from the finger tips to beyond the wrist. The color was not uniform but presented a mottled appearance, with areas of lesser cyanosis. The nails were yellow, exhibiting none of the normal pink hue. The soft tissues of the hand, particularly the terminal phalanges, were very tense. There was only slight ability to flex the fingers. The hand felt cold to touch, and sensation was numbed. The left hand gave a mottled appearance of blue and pink, interspersed. The tissues were less tense, sensation was present, and moderate flexion of the fingers was possible. Grolnick considered the case one of early gangrene, especially of the skin, due to immersion in the caustic oxalic acid solution, the effect probably being similar to that produced by continued local applications of strong phenol solutions. He prescribed hot epsom salt baths, dry heat, and wollen wrappings around the hands. The next day the patient stated that the pain was nearly gone. He was able to move the fingers on the left hand freely, and had about 50 per cent flexion in the fingers of the right hand. In a few more days he had no more discomfort and returned to work.

MICROSCOPIC AND SEROLOGIC TESTS FOR SYPHILIS. W. LEVIN, Northwest Med. **28**:517 (Nov.) 1929.

Levin favors the Kahn test. In more than 20,000 specimens tested (including serums and spinal fluids), the Kahn test has consistently "picked up" more positive reactions than the Wassermann. Out of 434 specimens examined by the dark field 188, or 43 per cent, yielded *Spirochaeta pallida.*

HISTOPATHOLOGY OF LEPROSY UNDER LOCAL INFILTRATION. J. O. NOLASCO, J. Philippine Islands M. A. **9**:347 (Oct.) 1929.

Nolasco made a histologic study of the changes in leprotic lesions following their infiltration with the mixed ethyl ester of *Hydnocarpus wightiana* oil, 0.5 per per iodine. Three lots of tissue from eleven patients were studied; one lot after the months of the infiltration treatment and the other two after one and four or five injections, respectively. All the patients had previously been given intramuscular injections for periods ranging from ten weeks to eighty-eight months. Before the infiltration treatment was begun two apparently similar lesions were selected and one was treated, the other being kept as a clinical control. Intra-

muscular injections (from 2 to 3 cc. a week) were also given during the course of the local treatment, during which time there was little change in the appearance of the lesions that were not infiltrated. The number of infiltrations given varied from seventeen to thirty-two. In the lesions treated for ten months the amount of leprous tissue was markedly reduced. The fact that although intramuscular injections were also given the untreated lesions remained clinically unchanged or only slightly improved, whereas the treated ones subsided markedly, indicates clearly a local favorable effect of this method of therapy.

EFFECT OF RADIANT HEAT ON PRODUCTION OF ACTINIC ERYTHEMA. F. M. SHATTOCK and M. D. WALLER, Lancet **2**:917 (Nov. 2) 1929.

Experiments were made by Shattock and Waller to ascertain whether the addition of "radiant heat" rays had any appreciable effect, either synergic or antagonistic, on the production of actinic erythema, and whether, if any such effect is noted, it can be attributed to some "physiologic" action or "physical" cause. They found that heating tissues by radiation or by conduction (radiator, hot water in vessel) after exposure to ultraviolet radiation diminishes — or suppresses — the actinic erythema and delays its appearance. Heating of tissues by radiation or conduction before exposure to ultraviolet radiation increases the actinic erythema. The time of appearance of the actinic erythema is not appreciably influenced. Heat (radiant heat or hot air draft) applied simultaneously with ultraviolet irradiation diminishes — or suppresses — the actinic erythema and delays its appearance. Differences in color as well as differences in depth of reaction are noticeable. The actinic erythema of the heated skin is more scarlet or vermilion (similar in color to the primary erythema), as compared with the actinic erythema produced by the mercury vapor or water filtered carbon arc light, which is more crimson or carmine. Differences of from 20 to 30 per cent of exposure to ultraviolet rays are necessary to produce visual differences in the erythema. Smaller percentage differences of exposure to a given source of radiation will give appreciable differences in the latent period — i. e., the time elapsing before the appearance of erythema. The diminution of actinic erythema by heating the tissues, either with radiant heat or by conduction, during ultraviolet irradiation, suggests a "physiologic" rather than a "physical" cause for the diminution observed. The fact that at least equally satisfactory diminution of erythema can be obtained by heating after irradiation with ultraviolet rays cannot be explained on the basis of physical interference or antagonism of the rays. The observed action of ultraviolet rays on the sensitiveness of the skin to thermal stimulation appears to be immediate. It is suggested tentatively that this action may be a factor in determining the degree of actinic erythema in cases in which heat is applied simultaneously or after ultraviolet irradiation.

INFECTIVITY OF ERYTHEMA NODOSUM. J. O. SYMES, Lancet **2**:1033 (Nov. 16) 1929.

The nature of the infective agent in erythema nodosum is at present unknown. On the continent the view is widely held that this disease is a modified form of tuberculosis, but in England and in America it is increasingly regarded as a streptococcal infection. Whatever the organism may be, Symes shows that its activity in all European countries is greatest in March and April, and this groups it with such diseases as pneumonia, streptococcus infection, tuberculosis, and epidemic encephalitis, for which the winter months, by the absence of sunlight, prepare the soil. Infection takes place through the tonsils, and it is probable that it is in these organs and in the nasopharynx that it lies dormant for weeks or months.

USE OF BISMUTH IN TREATMENT OF CONGENITAL SYPHILIS. T. M. LING, Lancet **2**:1034 (Nov. 16) 1929.

Ling asserts that it is possible to render serologically negative a certain proportion of apparently Wassermann-fast patients with congenital syphilis by

means of bismuth, and that its use is not accompanied by any untoward symptoms, apart from the occasional occurrence of temporary albuminuria. It is suggested that these results are due to the fact that *Spirochaeta pallida* has become resistant to arsenic and mercury after prolonged treatment.

BLOOD CHANGES IN EARLY STAGE OF VARICELLA AND IN PAROXYSMAL STAGE OF WHOOPING COUGH. A. SALVADEI, Clin. Pediat. **11**:1048 (Nov.) 1929.

Salvadei studied the changes in the blood in sixteen children, aged from 3 to 5 years, during the initial period of varicella. Five of them were in the paroxysmal stage of whooping cough. The blood was taken from the thumb before the children breakfasted. The analysis was made twenty-four hours before the appearance of the eruption of varicella, and during the first twenty-four hours of the eruptive stage. The author concludes that varicella, either by itself or when associated with whooping cough, modifies the blood with specific characteristics. These modifications, which were more marked in the blood of patients with whooping cough, are (1) absolute leukopenia, (2) neutropenia and (3) lymphocytosis, regularly associated with an increase of the basophilic and acidophilic cells of the blood.

VALUE OF MEINICKE CLARIFICATION TEST IN SERODIAGNOSIS OF SYPHILIS. M. MIRAGLIA, Pediatria **37**:1051 (Oct. 1) 1929.

Miraglia found the Meinicke clarification test simple in its technic and easy to interpret. His observations lead him to regard it as more sensitive and, which is more important, as more specific than the Wassermann test. Tuberculous infection and exanthematic diseases do not seem to influence positively the Meinicke clarification test, although in certain cases the nonspecific positive results with the Wassermann test are to be attributed presumably to their influence. The Meinicke clarification test deserves, therefore, wide application, particularly in childhood, in which tuberculous infection occurs so frequently. One objection, however, to its wide employment in the case of children is the fact that it requires a relatively large amount of blood serum (0.70 cc.).

MECHANISM OF MODERN FEVER THERAPY. J. VONKENNEL, Deutsches Arch. f. Klin. Med. **165**:180 (Oct.) 1929.

Vonkennel states that in malaria therapy the normal vesiculation time of eleven or twelve hours (the time elapsing between the application of a cantharides plaster to the thigh and the appearance of vesicles) is reduced during the height of an attack of fever to five or four hours. Following the crisis, the vesiculation time increases to five or six hours and in the fever-free interval it remains at from six to seven hours. On the basis of these facts the author concludes that the increased permeability of the cells of the human organism is an important factor in the action of modern fever therapy.

EVIDENCE THAT NOURISHMENT CANNOT BE ABSORBED BY THE SKIN. H. WINTERNITZ and H. NAUMANN, Deutsche med. Wchnschr. **55**:1828 (Nov. 1) 1929.

Winternitz and Naumann discuss the various methods for artificial nutrition. They point out that rectal, subcutaneous or intravenous administration of food supplies the body only with water and carbohydrates because proteins and fats are not absorbed by the organism when given in this manner. Stejskal advocates inunction with a nutritional preparation that contains 50 per cent of fats, 37 per cent of carbohydrates, 5 per cent of proteins and also vitamins. He asserts that with this method of application up to 1,400 calories can be absorbed by the skin. The authors, however, point out that the anatomic structure of the skin is unfavorable for the assimilation of foods. Because the skin is saturated with fats of the

cholesterol type, only those substances can be absorbed which can be dissolved in these fats. On the other hand, there is the possibility that the nutritional substance is absorbed by the cutaneous glands or by the hair follicles. Intake by the surface, however, does not prove that the substance is really assimilated by the body. In order to determine whether the skin absorbs fats, the authors made various tests. They come to the conclusion that the skin is not suited for the absorption of foods and that nutrition through the skin is therefore not possible. The question whether minute quantities of fats, carbohydrates and proteins are absorbed by the skin under certain conditions is of pharmocologic and clinical interest. However, for the purpose of nutrition this route is valueless.

PATHOGENESIS OF CONGELATION URTICARIA. A. PERUTZ, S. BRUGER and A. GRÜNFELD, Klin. Wchnschr. **8**:1999 (Oct. 22) 1929.

Congelation urticaria, according to Perutz et al., is a dermatitis that develops after contact with ice, with cold wind or with cold water. Wheals appear and a strong itching sensation is felt. Following a longer or shorter latent period, a nettle rash develops which is either limited to the areas that were exposed to the cold or spreads over larger areas. Two cases of congelation urticaria are described in detail. In order to determine the pathogenesis of this disease, careful tests and experiments were made on the two patients. In neither of these two cases were indications found which characterize congelation urticaria as an allergic dermatitis. Eosinophilia was not present. Contact with cold did not produce either a decrease in leukocytes or hemoglobinuria. Attempts to produce hemoclastic crisis gave negative results. The potassium and calcium contents of the blood were normal and did not show changes after an urticarial eruption. However, there existed a hypersensitivity of the thermoreceptor apparatus. Accordingly, the authors think that a vasoneurosis of the thermoreceptor apparatus is the main pathogenic factor in congelation urticaria.

PROGNOSIS AND TREATMENT IN BURNS. C. KREIBICH, Med. Klin. **25**:1656 (Oct. 25) 1929.

Kreibich states that death from burns is the result of poisoning. The coagulated protein has a toxic effect. The prognosis in a case of burn is determined by the size of the area and also by the degree of tissue destruction. The author distinguishes five degrees of burning; namely, erythema, formation of blister, necrosis of the upper portion of the papillae of the corium, necrosis of the entire papillary layer, and carbonization. The third and fourth degree burns have the greatest toxicity because the scab is soft and consequently the poisonous substances are easily absorbed. In the fifth degree the danger of poisonous intoxication is somewhat less because in carbonization the crust is dry and the toxins are not so easily absorbed. In the third, fourth and fifth degree burns death is likely to result even if only minor portions of the body are affected. A fourth degree burn extending over one eighth of the body surface may cause death, whereas a second degree burn may cover one third of the entire surface and yet the patient may recover. In the treatment of burns one should attempt to remove the toxins from the body. Some authors advise blood transfusion. However, the author recommends infusions with solutions of sodium chloride. He describes the case of a patient in whom one fourth of the body surface was destroyed by third and fourth degree burns. The patient recovered after the intravenous administration of a solution of sodium chloride by means of continuous drop infusion.

THERAPEUTIC USES OF CATHODE RAYS IN SKIN DISEASES. W. BAENSCH and R. FINSTERBUSCH, Strahlentherapie **33**:399 (Aug. 26) 1929.

Baensch and Finsterbusch first discuss the nature and production of cathode rays and the effect of the rays on plants, bacteria and animals. The experiments on both plants and animals proved that the biologic action of cathode rays is

limited to the surface. The authors therefore confined their use of cathode rays to the treatment of diseases of the skin. They obtained good results particularly in cancroids (even in those refractory to roentgen treatment), lupus exulcerans, verrucous tuberculosis, chronic eczema, warts and localized psoriasis. In lupus tuberosus, lupus carcinoma and infected slowly healing wounds, however, the results were unsatisfactory.

ADDITIONAL INDICATIONS FOR USE OF GRENZ RAYS IN DERMATOLOGY. H. FUHS and J. KONRAD, Strahlentherapie **33**:479 (Aug 26) 1929.

Fuhs and Konrad obtained good results with Grenz rays in the treatment of one case of Darier's disease, one case of atypical palmar ichthyosis, three cases of chronic lichenoid pityriasis, one case of acute varioliform pityriasis, one case of vascular poikiloderma (Jakobi), three cases of Spiereg's tumor and two cases of Durand-Fevre's disease. In all these cases the pathologic condition had been refractory to other forms of treatment (even to roentgen irradiation) but retrogressed in a relatively short time under treatment with Grenz rays.

BLOOD PICTURE IN PARESIS WITH ESPECIAL REGARD TO LEUKOCYTE COUNT BEFORE AND AFTER MALARIA INOCULATION. A. STENDER, Ztschr. f. d. ges. Neurol. u. Psychiat. **121**:255 (Aug. 6) 1929.

On the basis of review of the literature and his personal experience in forty-five patients with paresis in whom blood counts were made, Stender concludes that treatment with neoarsphenamine does not have any influence on the blood picture. However, malariotherapy restored the preexisting lymphopenia in one third of the cases to a normal count. In the other patients having a normal or an increased number of leukocytes, malariotherapy caused a slight leukocytosis, which was followed by a normal count in cases also showing clinical improvement. According to Stender, the occurrence of either lymphocytosis or lymphopenia after malariotherapy is prognostically unfavorable.

PRECARCINOMA. H. T. DEELMAN, Ztschr. f. Krebsforsch. **29**:307 (July 10) 1929.

Deelman defines precarcinoma as a pathologic condition of cells and tissues that eventually results in or may result in a malignant growth. The term has been used for a large number of pathologic processes in some of which the changes rarely result in a malignant growth; in these cases it is not known whether or not the malignant growth appears spontaneously. The author believes that the term precarcinoma should be restricted to processes in which the malignant growth appears spontaneously. The leukoplakia that occurs in the upper portion of the respiratory and digestive tracts is to be considered a true precarcinomatous change. At the periphery of the carcinoma that develops in leukoplakia there occurs the gradual transition from epithelium to tumor; here is present the morphologic substratum of precarcinoma in its final development. The epithelium in the patch of leukoplakia is to be regarded as a first stage of precarcinoma.

GROWTH OF CANCER IN MICE FOLLOWING ADMINISTRATION OF IRRADIATED ERGOSTEROL. L. BARELLI, Ztschr. f. Krebsforsch. **29**:376 (July 10) 1929.

Barelli reports that the growth of adenocarcinomas in mice is inhibited by the administration of antirachitic vitamin in the form of viosterol (irradated ergosterol).

SENSITIVITY OF NORMAL AND OF TUMOR TISSUES TO MESOTHORIUM AND ROENTGEN IRRADIATIONS. H. LASER and L. HALBERSTAEDTER, Ztschr. f. Krebsforsch. **29**:411 (July 10) 1929.

In experiments in which cultures of mouse cancer and rat sarcoma and control cultures of normal tissues were subjected to mesothorium and roentgen irradia-

tions, Laser and Halberstaedter found that the absolute sensitivity to irradiation was not greater in the tumor tissues than in the normal tissues. In all of the experiments the effect of the irradiation seemed to be dependent on the rate of growth of the tissues.

CAUSE OF CANCER OF PENIS IN CHINA. E. A. DORMANNS, Ztschr. f. Krebsforsch. **29**:435 (Aug. 3) 1929.

In a period of eighteen months in China Dormanns received for examination five specimens of cancer of the penis. Three of the specimens had been removed from men aged 24, 26 and 34 years, respectively. In the microscopic examination of the specimens the author noted that in all of them the cancer had developed on a greatly inflamed skin. In four of the specimens the microscopic changes resembled the changes found in experimental tar cancer. Extirpated inguinal lymph nodes had been sent with two of the specimens but they were found to be free from metastases. In searching for an explanation of the frequency, occurrence in young men and resemblance to experimental tar cancer of cancer of the penis in China, the author noted that gonorrhea, syphilis and particularly chancroid are treated there by the local application of highly irritant substances. Owing to his inability to obtain any of these substances he was unable to substantiate experimentally his suspicion with regard to their carcinogenic properties.

CANCER IN YOUNG PERSONS. H. JUNGHANNS, Ztschr. f. Krebsforsch. **29**:623 (Sept. 6) 1929.

Junghanns states that of 4,192 cancers that were found in 36,408 necropsies, six occurred in persons (two males and four females) aged less than 20 years.

NODULES IN ACUTE AND SUBACUTE RHEUMATISM. C. DE LANGE, Nederl. Maandschr. v. Geneesk. **15**:571, 1929.

De Lange brings out that nodules associated with rheumatism occur mostly in the subcutis but also in the galea aponeurotica, the joint capsules, the pia mater, the heart muscle and the skeletal muscles. The size varies from that of a pea to that of a walnut. The skin over them does not change in color ordinarily, though sometimes there is a slight redness. Often their localization is more or less symmetrical. They develop at times in a single night. In the first stage they are somewhat painful; later little pain is noticed. The nodules may be palpable and visible for weeks, but they may also disappear rather suddenly. The elbows, the knees, the ankles, the metacarpophalangeal joints, and the spinous processes of the vertebrae are predilection points. De Lange's studies on a series of cases leads her to conclude that there is no adequate justification for setting up "nodose rheumatism" as a morbid entity. Nodules in association with rheumatism in children are comparatively common. The presence of many large nodules is very general in grave heart disorders (endocarditis, pericarditis) and is an indication of an unfavorable prognosis.

TREATMENT OF CONGENITAL SYPHILIS WITH SO-CALLED INOCULATION MALARIA. G. ÅHMAN, Hygiea **91**:678 (Oct. 15) 1929.

Åhman made forty inoculations in thirty-six cases, mostly refractory and unfavorable in prognosis. The results seem to him to encourage continued attempts on a larger scale.

PRIMARY CUTANEOUS GONORRHEAL INFECTION, PANARITIUM FOLLOWED BY GONORRHEAL LYMPHANGITIS, GENERAL INFECTION, AND POLYARTHRITIS. V. GENNER and P. SCHULTZER, Hospitalstid. **72**:764 (July 11) 1929.

In Genner and Schultzer's case in a dermatologist, direct cutaneous transmission from a patient occurred through a barely visible lesion in the epidermis. A

panaritium with lymphangitis resulted, with metastatic spread in the form of a polyarthritis. The character and course of the joint condition were typical of gonorrheal arthritis. The gravity of this case with its complications is a warning, especially to dermatologists, to bear in mind the possibility of a gonorrheal panaritium.

RADIUM TREATMENT OF ANGIOMAS. J. NIELSEN, Ugesk. f. Læger **91**:795 (Sept. 19) 1929.

Nielsen's material consists of 415 angiomas treated at the Copenhagen radium station and examined from one to fifteen years later. Most of the patients were children, 261 under one year. Of the 354 cavernous angiomas, cure was effected in 90 per cent; also in an additional 7 per cent with results more or less compromised by secondary effects, the doses having been stronger than elective. Of the fifty-five telangiectases, four of coin-size were cured; of the fifty-one extensive capillary angiomas, improvement was noted in only 40 per cent. The author believes that if the treatment was begun as early as possible (days or weeks) after birth, the results might be improved. In the six venous cirsoid angiomas there was improvement in only one. The fundamental principles of the method used are: always suberythemal, elective doses and never new treatment until the effect of the preceding treatment is surely past. The excellent cosmetic results are emphasized. The radiosensitivity of angiomas is greatest at birth. No disturbances of development were observed even in the very young. Except in small and superficial, mainly stationary angiomas, radium therapy must be considered the method of choice in the treatment of angiomas. In plane nevi, radium therapy is only partly successful.

BISMUTH INFARCTS AND THEIR PREVENTION. S. LOMHOLT, Ugesk. f. Læger **91**:921 (Oct. 24) 1929.

Lomholt found in the literature from 1924 to 1928 fifty cases of bismuth infarcts in the buttocks following intramuscular injection. He describes the nine cases observed by him in about 20,000 injections; there was no permanent infiltration. In addition to care that after insertion of the cannula blood is not aspirated into the tube, he advocates a slow, slight withdrawal of the cannula during injection to lessen the danger of fluid containing bismuth being forced into a lacerated blood vessel.

FULMINANT ERYSIPELAS. E. HJORT, Norsk. Mag. f. Lægevidensk. **90**:970 (Sept.) 1929.

Hjort describes a case of violent streptococcic infection diagnosed as fulminant erysipelas, fatal in thirty-three hours.

Society Transactions

NEW YORK ACADEMY OF MEDICINE, SECTION OF DERMATOLOGY AND SYPHILIS

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May, 1929

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MYCOSIS FUNGOIDES. Presented by DR. MCCAFFERTY.

M. J. R., a white man, aged 41, an automobile mechanic, from the Polyclinic Hospital, was seen on May 6, 1929. At that time he complained of lumps in the skin and a swelling of the penis, which had been present for one month. He presented rounded and oval shaped, painless tumors confined principally to the thighs. They ranged in size from that of a split pea to that of a small fist, were purplish red, moderately firm and had no tendency to break down. They were elevated above the level of the skin as much as 15 cm. The penis, especially the glans, was red, swollen and indurated. There was a subcutaneous, slightly painful tumor mass at the lateral aspect of the right forearm. The Wassermann test was made and blood count taken, but the report had not been obtained.

DISCUSSION

DR. ANDREWS: I think that the eruption is leukemia cutis. The color and consistency of the tumors suggest that to me, as does also the condition of the penis, which is edematous and superficially ulcerated, very similar to the case of Hodgkin's disease with lesions on the penis, which Dr. Sharlit presented a year ago. On account of the short duration, multiple tumors, the typical color and consistency, I favor the diagnosis of leukemia cutis.

DR. LEVIN: I agree with the diagnosis made by Dr. Andrews. Clinically, the tumor-like masses would suggest the diagnosis of leukemia rather than that of mycosis fungoides.

DR. MCCAFFERTY: In view of the fact that the patient appeared only yesterday afternoon it has been impossible to work up the case properly. It unquestionably falls into the lymphoblastoma group, and that is about as close as one can come, at this time.

LEUKEMIA CUTIS. Presented by DR. FEIT.

The patient said that the eruption had started with a rash on the scalp two years previously, which had cleared up while taking some medicine internally. For a year no eruption had been present. Then a similar rash appeared again on the scalp, but disappeared in four days.

Nearly the whole of the scalp was infiltrated, was of a bluish-red color, and in its posterior part was studded with yellowish-red papules, some of which were densely set, forming a patch about the size of a quarter. They were raised above the level of the normal skin. There was a similar infiltration covering in batlike manner the nose and adjacent parts of the cheeks. The surface showed numerous dilated venules. The anterior part of the nose was covered with tumor-like, brownish-red tubercles which were soft, giving the impression of being filled with fluid (cystic). Pricking with a needle, however, did not evacuate much fluid; only a droplet of blood could be expressed.

There was no enlargement of the liver, spleen nor any general adenopathy. The blood count showed 34,000 white blood cells and 86 per cent lymphocytes (300 cells were counted). Microscopic examination showed the epidermis to be of uniform thickness; there was slight hyperkeratosis and flattening of the papillary processes. Scattered through the derma and down to the subcutaneous tissue were large groups of mononuclear cells of the lymphoid type. There was some brownish pigment in the depth of the infiltration, the cells giving the impression of an invasion rather than an inflammation. The histologic picture might be that of a lymphatic leukemia.

The differential white blood count showed: polymorphonuclears, 10 per cent; lymphocytes, 63 per cent; lymphoblasts, 63 per cent; eosinophils, 1 per cent and many degenerated nuclei.

HODGKIN'S DISEASE OF THE SKIN. Presented by DR. CORNELL.

H. R., a boy, aged 15 years, came to the Post-Graduate Hospital ten days before presentation. He said at that time that about one year previously he had noticed a general itching of the skin which had gradually become worse.

On examination, there was found to be a generalized papulonecrotic eruption with some urticarial lesions and pigmentations. There were many enlarged lymph glands on the sides of the neck and in the sternoclavicular region. There was also axillary adenopathy. The itching was quite severe at times, and interfered with the sleep of the patient.

A roentgenogram of the chest taken in the postero-anterior direction showed a large tumor mass in the mediastinum. It was believed this was a glandular mass and either lymphosarcoma or Hodgkin's disease.

Examination of the blood showed the hemoglobin to be 87 per cent; red blood cells, 4,800,000; white blood cells, 34,000; polymorphonuclears, 85 per cent; lymphocytes, 13 per cent and eosinophils, 2 per cent. No abnormal cells were seen.

Microscopic examination of a frozen section of the node from the neck showed a considerable amount of fibrosis. The normal structure of the node was lost with disappearance of nodules and diffused distribution of the lymphoid cells. There were a few eosinophils. There was no evidence of tuberculosis, nor did the section suggest sarcoma. The changes corresponded most closely with those seen in Hodgkin's disease. There were a few large cells of the Dorothy Reed type.

The results of the Wassermann test were negative.

DISCUSSION

DR. LEVIN: This case should be included with the leukamides rather than as a true leukemia of the skin. The lesions which are present are those due to the toxic effect of the general condition rather than to leukemic infiltration. I have seen only once a true Hodgkin's disease of the skin, and in that case, the dermatologic condition was due to an invasion from the underlying lymph nodes. Leukamides are fairly common, while true Hodgkin's disease of the skin is very rare.

DR. CANNON: I had a patient who died in the City Hospital with Hodgkin's disease about a year ago. He had many true lesions of Hodgkin's disease of the skin and mucous membranes of the mouth.

DR. RULISON: I have looked up the literature on this disease, and so far I have failed to find a case in which this prurigo-like eruption showed true Hodgkin's disease on histologic examination. It seems, as pointed out by Dr. Fox in an article he published in 1920, that there are two types of eruption in Hodgkin's disease, i. e., one which is usually pruritic and often prurigo-like which does not show the true Hodgkin's structure and the other, usually tumor-like, which shows the true Hodgkin's structure.

ACRODERMATITIS CHRONICA ATROPHICANS. Presented by DR. GROSS.

I. W., a white woman, aged 56, born in Russia, was first seen at the clinic of the Hospital for Joint Diseases on the day of presentation. The disease was of many years duration. The patient had had seven children, four of whom had died in early childhood. There had been no miscarriages. The patient's menopause had occurred when the patient was 46. Urinalysis was negative.

There was a diffuse idiopathic atrophy present on both legs and thighs reaching to the groin. There were, also, numerous lesions of macular atrophy. On both thighs especially on the left there were several flat tumors varying in size from that of a lentil to that of a dime, of firm consistency and yellowish brown in color. Some of these lesions appeared to have developed in an area of macular anetodermia. On the right forearm there was an ulnar band in an erythematous atrophic stage.

LUPUS ERYTHEMATOSUS AND MYCOSIS FUNGOIDES. Presented by DR. FEIT.

M. F., from the New York Skin and Cancer Hospital, said that the eruption first appeared on the left part of her nose five and one-half years previously, and that after ultraviolet rays had been applied, the disease began to spread. Carbon dioxide snow was later applied. There seemed to be no active lesions in the area treated, which showed a good cosmetic result.

The eruption for which the patient was presented started on the back of the hand five and one-half years previously, gradually involving the left half of the body, but no lesions appeared on the right side, according to the patient's definite statement. The patient also gave a history of her hair having fallen out and coming in again, which she attributed to roentgen therapy. All over her body were configurated, red patches which showed definite infiltration and were covered with scratch marks. There was a thickening of both eyelids and of the supra-orbital region which stood out quite prominently. The patient suffered from severe itching. The patches had not been treated for the past fifteen months, but had been treated for a year with the roentgen rays. About thirty injections of a gold preparation had been given which, according to the patient, had not improved her condition.

The blood count taken Dec. 29, 1927, showed 5,000,000 red blood cells; polymorphonuclears, 73 per cent; lymphocytes, 23 per cent and transitionals, 4 per cent.

DISCUSSION

DR. HOWARD FOX: I think that this is an undoubted case of mycosis fungoides from the clinical standpoint. There is a characteristic difference in the degree of infiltration in different lesions and in different parts of individual lesions. It is unusual, however, to see so much excoriation in this disease. Although the patients often complain bitterly of itching, they do not tear the skin, as a rule, by scratching.

DR. WALZER: The only reason for the diagnosis of lupus erythematosus is the scars on her face and the fact that she had been treated for lupus a number of years before. Is it not possible that the mycosis fungoides started on her face and simulated lupus? It is well known that mycosis may begin with lesions simulating almost any dermatologic condition.

DR. FRASER: My impression is that we are dealing with one condition, namely, mycosis fungoides.

DR. FEIT: This patient was treated for years for a discoid type of lupus erythematosus at the New York Skin and Cancer Hospital. Later, she developed mycosis fungoides which was histologically verified. Hallopeau reported a case in which he first thought he was dealing with mycosis fungoides but later saw the case develop into a disseminated lupus erythematosus.

MELANOCARCINOMA. Presented by DR. ABRAMOWITZ.

E. W. W., a girl, aged 19 years, a packer of cosmetics, presented herself at the clinic of the Israel-Zion Hospital. She had had a small pigmented mole the size of a pinhead removed from the skin over the upper border of the left scapular region about one year previously, by a physician who used either fulguration or electrodesiccation. The lesion promptly returned and had grown quite slowly for a year. The growth was the size of an olive, pitch black in color and consisted of several peasized nodules. At its lower pole a scar was present where the operation had been performed. A small, slate-black mole was also present on the left side of her chin.

DISCUSSION

DR. ANDREWS: I think that is a remarkable lesion. The interesting feature is that the mole from which it arose was black, hairless and flat; it was not a soft brown mole. Many of us have the impression that black, flat moles are more commonly the sites of melanocarcinoma. This case tends to confirm such impression. The pathologists are inclined to think and most of us agree, that potentially any mole may form melanocarcinoma but seldom do we know the exact clinical type of mole antecedent to the melanocarcinoma.

DR. POLITZER: It seems to me that the most interesting feature in this case is that the patient has been treated and there is a recurrence in loco. I should like to hear something about the treatment employed.

DR. ABRAMOWITZ: Presumably the original lesion must have been of the same type as the one on the left side of the chin. That lesion is definitely slate-black. In my opinion it is a type of lesion which should be let entirely alone or adequately excised. While I labeled this growth melanocarcinoma, which I believe it is, it has not been confirmed by biopsy.

PITYRIASIS RUBRA PILARIS. Presented by DR. MITCHELL.

J. T., a boy, had first been seen in March, 1926, when he was 3 years old. His mother said that he had been severely burned by a gasoline explosion one year before, and following the accident had developed a general red scaling eruption. The examination at that time showed an exfoliative dermatitis affecting his entire skin except an area on each instep. He had yellowish red, thickened, scaling, cracked palms and some loss of hair on the scalp and eyebrows. In May, 1926, he first showed the black topped follicular plugs on his fingers and toes.

He was given thyroid extract and in February, 1927, the skin was entirely clear. The thyroid extract was continued until May, 1928, and he was seen at short intervals until January, 1929, when a few swollen follicles were noted about his neck and hands with some roughness of the skin over the knees and palms. He was given thyroid extract again but the eruption became practically generalized again with the follicular plugs appearing later.

At the time of presentation, the eruption on his body and face was clearing, but the characteristic plugs could be seen on the fingers and forearms.

DISCUSSION

DR. HOWARD FOX: Has any one ever seen a younger child than this with pityriasis rubra pilaris? The diagnosis in this case is certainly plain.

NODULAR SYPHILIS (PREVIOUSLY PRESENTED). Presented by DR. ABRAMOWITZ.

Y. L., a man, aged 25, born in China, was admitted to the clinic of the New York Post-Graduate Hospital on March 18, 1929, with three large areas of sharply defined patches, one over the nose and one over each cheek. These were sharply defined, bluish red with adherent scales. The border was distinctly raised and infiltrated. There was considerable pigmentation. The patient was presented at the April meeting of the section as having lupus erythematosus.

Physical examination showed the heart and lungs to be normal. The results of the neurologic examination were negative. Serologic examination on March 18, showed negative reactions to the Wassermann and Kahn tests. On April 29, the reactions to both tests were again negative. From April 3 to April 26, the patient received three injections of neoarsphenamine and four injections of a suspension of bismuth salicylate oil. On April 19, the infiltration began to disappear, and on April 23, considerable improvement was noted. On April 26, the lesions on the cheek were flattened out except for a small band beneath the right eye. The histology was not definite but it suggested syphilis.

DISCUSSION

DR. ABRAMOWITZ: I think that this is the third case I have seen personally in which a diagnosis of lupus erythematosus had been made and syphilis was later proved. In one particular case, presented before this section, the patient was treated for twenty years for lupus erythematosus. The face was disfigured from radium, carbon dioxide snow and other agents. The results of several Wassermann tests had been negative. We observed a 4 plus Wassermann reaction, and antisyphilitic treatment cleared up some lesions that were present. The lesions on the patient presented here cleared up entirely in too short a time for them to be considered other than syphilitic. This case is educational because we read many reports wherein patients with lupus erythematosus are helped either by the administration of bismuth, mercury or arsphenamine, and I think it is incumbent on us, no matter how typical a case of lupus erythematosus appeared to be, that the diagnosis should be confirmed by histopathologic report and repeated Wassermann tests. Some of the cases will be found to be syphilis and not lupus erythematosus.

FIBROID SUBCUTANEOUS SYPHILODERMAS. Presented by DR. BECHET.

E. F. A., a woman, aged 34, said that five years previously she had first noticed tumors beneath both elbows. In the next few years a considerable number of new ones appeared extending down the forearms and involving the hands. The growths had developed exceedingly slowly. She presented for examination a number of hard tumors varying in size from that of a filbert to that of a walnut on the forearms and hands. Most of them were freely movable and were covered with normal skin, but a few seemed to be attached to a tendon sheath. They were painless on palpation. Roentgenograms showed no definite bone or joint pathology. The Wassermann reaction was 4 plus.

POIKILODERMA-LIKE CHANGES OF THE SKIN. Presented by DR. GROSS.

R. S., an unmarried white woman, aged 28, born in Russia, said she had first noticed her eruption seven years previously. About that time she had received roentgen therapy for hypertrichosis of the face. No roentgen treatment had ever been applied to her body.

When first seen at the Vanderbilt Clinic she presented diffuse atrophy of both cheeks with numerous telangiectases and in places scarlike induration. On the outer aspect of both breasts were large areas studded with telangiectases; similar patches, less marked, were noted on the thighs, and in some areas there was atrophy. On the abdomen were pronounced striae distensae in which dilated blood vessels were visible. The hair of the scalp was thin and sparse with circumscribed scars, especially on the vertex. There was a definite exophthalmos. The skin was rather dry and scaly in places. There was an excessive growth of hair on the chest, abdomen, shoulders, legs and thighs. The skin, in general, showed a lack of tonicity. The pubic hair was of masculine type. The thyroid gland was possibly slightly enlarged. Blood pressure was 140 systolic and 90 diastolic.

Roentgen examination of the chest and skull showed the sella turcica to be somewhat large and its floor was very thin, but did not show definite erosion. The superior border of the posterior clinoid process, especially on the left side,

could not be made out. The observations were very suggestive of a pituitary disturbance, probably a tumor. The roentgenogram of the chest revealed no shadow to suggest thymic enlargement. The shape of the thoracic cage was small and narrow and the diaphragm was quite high on both sides, covering the lower border of the heart on the left and right side. The lung fields were clear.

The basal metabolic rate was minus 15. Hypothyroidism and hypopituitarism was present due to a possible benign tumor of the pituitary gland.

DISCUSSION

DR. HOWARD FOX: It seemed to me that the lesions on the breast closely resembled angioma serpiginosum, and were similar to those on the breast in a patient of mine included in Dr. Wise's study of this disease. It was a curious coincidence that the patient showed radiodermatitis of the face which was apparently due to treatment for hypertrichosis by the roentgen rays.

DR. WISE: I agree with Dr. Fox that the lesions on the breast resemble angioma serpiginosum. Taking the eruption as a whole, however, I do not think that such a diagnosis is applicable. A diagnosis of poikiloderma-like eruption would be acceptable, resembling as it does the type described by Jacobi. The lesions on the upper inner aspect of the arms were distinctly atrophic and presented linear striae. Taking the eruption as a whole, I should corroborate the presenter's interpretation of a polyglandular endocrine manifestation of the skin, but would hesitate to classify the case as poikiloderma atrophicans vasculare.

DR. CANNON: A few years ago I studied this case at the Vanderbilt Clinic. The patient presented the same clinical appearance at that time as she does now. We considered the skin condition due to a disorder of the pituitary gland, and roentgenograms taken of the skull showed an enlargement of the gland. Biopsies made of the atrophic skin showed only atrophy with absence of the elastic tissue, while the tissue removed from the red areas showed mainly telangiectases.

DR. LEVIN: This patient was at the Mount Sinai Hospital four or five years ago. At that time she presented cutaneous lesions similar to those observed this evening. The condition was considered as a vascular anomaly of the skin, associated with the disease of the pituitary gland. I also saw a similar case at the Montefiore Hospital which presented the identical cutaneous manifestations as well as the stigmas associated with disease of the pituitary gland.

DERMATITIS VENENATA (NICKEL PLATING SOLUTION). Presented by DR. FEIT.

J. F., a youth, aged 20, a jeweler had had an eczema-like eruption two years prior to presentation, at which time he first worked with nickel plating. This eruption disappeared in three months when the patient gave up handling nickel plating. Two and a half months before first being seen he had started to work in a jewelry shop where he handled nickel and other metals, and the eruption again broke out. When first examined, the fingers, backs of the hands, elbow flexures and popliteal spaces were involved. After three injections of sodium thiosulphate, the lesions completely disappeared from the arms and legs but remained on the hands and on the fingers. The patient was advised then to apply gauze saturated with nickel plating solution on his arm and to leave it there for twenty-four hours. He had to remove it after four hours because the itching was so severe, and when he came back to the clinic the same areas which had cleared up were involved with eczematous patches, which also appeared on the forehead and neck. After another week's treatment with sodium thiosulphate, the condition again cleared up, except for the hands and fingers.

Chemical examination of the blood before treatment showed sugar, 146 and chlorides, 466; after treatment, sugar, 103 and chlorides, 437; a third test reported sugar, 96.9 and chlorides, 475.

DISCUSSION

DR. HOPKINS: It seems to me that Dr. Feit's case ought to go definitely on record as a well proved case of occupational dermatitis due to nickel.

PEMPHIGUS VULGARIS. Presented by DR. CANNON.

I. C., a white man, aged 37, born in Russia, a furrier was first seen at the City Hospital on March 26, 1929, with a generalized eruption which had been present for about two and one-half months. Seven months prior to admission, he first developed ulcerations on the gums and buccal mucosa, and from there they spread to the hard palate and lips. The ulcerations persisted in these areas for about four months and then new lesions appeared in the groins and on the fingers, and following their appearance similar ones appeared rapidly over the rest of the body. He was treated by several private physicians and was hospitalized for about one month without relief. He was then sent to the City Hospital.

On admission, the patient appeared to be weak and extremely ill. He had a generalized eruption scattered over the face, trunk and extremities consisting of single and confluent circular and polycyclic lesions varying in size from that of a dime to that of a palm. Most of the lesions appeared as superficial ulcerations from the bases of which exuded a rather foul-smelling purulent discharge. Some of the sores were covered with thick brownish crusts, while scattered over the body were a few small vesicles, filled with serous and seropurulent fluid. In the groins, axillae, anterior portion of the neck and between the buttocks, the skin was red, sodden and elevated in warty rugae. There was also an offensive-smelling discharge from these regions. The lips were covered with red, crusted, painful lesions which made the opening of the mouth difficult. On the oral mucosa could be seen numerous superficial ulcerations some of which were covered with a grayish colored slough.

Roentgen examination of the lungs and gastro-intestinal tract gave negative results. The blood urea nitrogen was 15; sugar, 10, and the blood count showed 80 per cent hemoglobin, 3,700,000 red blood cells, 11,500 white blood cells, 85 per cent polymorphonuclears, 37 per cent mononuclears and 2 per cent eosinophils.

DR. FELDMAN: I think that I am the first one who saw this patient. He came to me about nine months ago, and at that time he showed bluish discoloration on the buccal mucosa on both sides together with large broken down bullae. There was involvement of the gums which was diagnosed as Vincent's angina and confirmed by microscopic examination. The case gave the impression of being that of a phenolphthalein eruption complicated by a Vincent infection. After about four weeks, the condition in the mouth was improved but had not cleared up entirely. At about the same time a vesicle developed in the axillary region, and the diagnosis of pemphigus vulgaris suggested itself. Yet the lesions in the mouth were so much like those due to phenolphthalein that one could not altogether discard that diagnosis.

At the present time there are some healed lesions on the chest that suggest the diagnosis of phenolphthalein eruption. On one of these patches three or four rings can be seen situated one within the other, giving the impression that new lesions have appeared in exactly the same location where a previous one had existed. There are, however, several lesions on the face that strongly suggest pemphigus. I am not ready to make a definite diagnosis at present, but I cannot give up the idea of it being a phenolphthalein eruption.

DR. HOWARD FOX: Dr. Pels is continuing his work in conjunction with Dr. Macht on the phytopharmacologic test and is anxious to get as many blood specimens as possible from cases of pemphigus.

DR. WISE: May I suggest that this patient be taken off all medication for awhile and that phenolphthalein be administered as a therapeutic test in order to discover whether the lesions flare up or not?

DR. CANNON: I realize that the diagnosis of pemphigus is not always an easy one to make, and when one recovers the nature of the disease is often questioned. This man apparently had a typical case of pemphigus with marked constitutional symptoms, mucous membranes of the mouth and the body covered with large bullae and extensive vegetating growths in the axillae and groin.

The pigmentation was only visible after the skin had healed, and we thought it could be explained by the arsenic and the ultraviolet light. While I am not ready to concede that the man is cured of pemphigus, I do believe that he has made a remarkable recovery considering the severity of his illness. I am taking him off all treatment and discharging him from the hospital tomorrow. I shall give him phenolphthalein to take later.

ALOPECIA ATROPHICANS PSEUDOPELADE, BROCQ. Presented by DR. MCCAFFERTY.

J. P., a white man, aged 33, born in Greece, had had a condition of the scalp for the past three years, which had been developing gradually. At no time had he noticed any pronounced inflammation or pustule formation. The general history was without bearing on the condition.

On examination, there were scattered over the scalp numerous irregularly shaped areas of alopecia, the largest of which was about the size of a quarter. Closer examination revealed complete atrophy of the hair follicles in these areas and on the periphery an occasional follicular pustule. Some of the hair seemed to be surrounded by slight hyperkeratotic cones and when extracted showed an edematous translucent hair sheath.

His son had had alopecia for four months.

ANEURYSM OF SUBCLAVIAN ARTERY; CLUBBING OF FINGERS. Presented by DR. CANNON.

A. B., a man, aged 52, was admitted to the City Hospital Feb. 14, 1929, with a diagnosis of subclavian aneurysm and syphilis. He first noticed the swelling in the left side of his neck about five years before, and he also gave a history of having had an apoplectic stroke a short time before that. The swelling in his neck had become larger, but had never bothered him to any extent. He said that he had had a chancre twenty-three years ago, and this was followed in a short time by a generalized eruption. He was a little vague about the duration of his hoarseness, stating at one time that it had been present only five years and stating later that he had been that way all his life.

Examination revealed a well developed and nourished man who did not appear to be very ill. In the left superclavicular space he had an irregularly outlined, fairly firm, but compressible, painless, pulsating tumor, which extended from the tip of the mastoid out almost to the end of the clavicle. There was an associated clubbing of the left fingers. The blood pressure in both right and left brachial arteries was the same. There was ptosis of the left eyelid and a complete paralysis of the left recurrent laryngeal nerve. The results of Wassermann tests of the blood and spinal fluid were both 4+.

GRANULOMA INGUINALE. Presented by DR. CANNON.

L. S., a negro woman, aged 21, born in the United States, was admitted to the City Hospital on April 24, 1929, on account of ulcerations on the vulva. She gave a history of having first developed lesions about five months prior to admission. The sores on the labia were extremely painful and tender. She also gave a history of a bilateral keratitis with diminished vision dating back to childhood.

On examination, on both labia, the inner aspect of the right thigh and extending up on the mons were numerous, slightly elevated, oval and circular lesions, varying in size from that of a pea to an olive. Their surfaces were covered with moist red granulation tissue from which there was a slight seropurulent discharge. These areas were extremely painful to the touch.

The results of examination of the blood were repeatedly negative. The Wassermann test of the spinal fluid was negative. Smears from an excised lesion showed abundant Donovan bodies.

GRANULOMA INGUINALE. Presented by DR. CANNON.

M. B., a negro woman, aged 21, born in the United States, who did housework, was readmitted to the City Hospital on March 26, 1929, on account of the recurrence of genital lesions and associated heart trouble. She had been under observation during the past three and one-half years. She was first seen at the Vanderbilt Clinic at which time she had a 4+ Wassermann reaction and marked swelling of both labia majora. She was treated over a long period with arsphenamine and mercury without any diminution in size of the labia. The labia were then amputated. During her stay in the hospital, Donovan bodies were demonstrated in smears from a portion of the excised tissue. Following the amputation of the labia, she was given tartar emetic, and the surgical wounds as well as adjacent ulcerations healed successfully, and the patient was discharged. She remained well for about four months, and then she noticed a recurrence of small ulcerations which gradually spread over the entire vulva and became so painful that she returned to the hospital for further treatment.

Examination showed that over the entire vulva were deep, irregular ulcerations varying greatly in size and shape. The bases were covered with a grayish slough, and in portions, unhealthy appearing granulation tissue from which exuded a serosanguineous discharge. The edges of these lesions were rolled and infiltrated, and among these ulcerations were a few scars from old sores. Lateral to the main sores were a few papules the size of a pea, some of which showed superficial erosions. Similar lesions extended posteriorly on the perineum and around the anus. Tartar emetic was given with improvement of the condition.

CORNU CUTANEUM. Presented by DR. ABRAMOWITZ.

S. G., a girl, aged 16, appeared at the Skin Clinic of the Post-Graduate Hospital in May, 1929. She presented on the left palm, near the thenar, a horny protrusion about one-half inch (1.27 cm.) long.

J. FRANK FRASER, M.D., *Chairman, Presiding*

MAX SCHEER, M.D., *Secretary*

Regular Meeting, October, 1929

ERYTHEMA FIGURATUM PERSTANS. Presented by DR. FEIT.

J. B., a printer, aged 45, born in Hungary but a resident of the United States for the past twenty-six years, had had an eruption for two years on the right hand, and for about two months on the rest of the body. He had been operated on for ulcerated stomach, and also had had sciatic rheumatism five years before presentation.

On the back of the right hand were three circular lesions varying in diameter from ¼ to 1½ inches (0.64 to 3.77 cm.), which were bluish red at the periphery and showed normal skin in the center. The margins were definitely infiltrated. There was no sensation. These lesions gradually developed during a period of two years. There were multiple lesions of a similar character on the chest and shoulders which were also infiltrated peripherally, as could be seen best on the stretched-out skin. There was never any scaling in these lesions. They started as firm, red papules which coalesced. Vesicles never formed. Slight pigmentation could be seen in the center.

DISCUSSION

DR. ABRAMOWITZ: In my opinion the condition is probably granuloma annulare. The lesions show a definite infiltrated border with a clear center and

progress too slowly for erythema annulare centrifugum. The latter disease is acute in its evolution, with new lesions appearing continuously.

A CASE FOR DIAGNOSIS (LUPUS PERNIO?). Presented by DR. ROSTENBERG.

I. K., aged 45, had an irrelevant history, except for an attack of erysipelas six years previously. A cervical gland had been removed, which was supposed to have been tuberculous.

The skin trouble started in June, 1929, when he noted a tiny lesion on the lobe of the left ear, which reached maximum development in a few weeks. During the previous winter he had been outdoors a great deal and thought it possible but did not know whether he had had his ear frozen.

The lobe of the left ear appeared greatly thickened and infiltrated. The subcutaneous tissues seemed tumefied and slightly sclerotic. The skin was of a dark, reddish color and appeared glossy. The lower pole of the lobe appeared hemorrhagic in color, and there seemed to be a few minute excoriations and slight scaling. There was no pain or itching, except a slight burning when the weather turned cool.

NOTE.—A biopsy taken subsequently showed a tuberculous structure.

DISCUSSION

DR. HIGHMAN: It seems to me that raising the question of lupus pernio in a dermatosis that began in June is rather straining at a gnat. It looks very much like lupus tumidus and that seems to me as good a diagnosis as any. Study of the lesion under the microscope would make further discussion unnecessary.

CREEPING ERUPTION. Presented by DR. MITCHELL.

William B., an American, aged 39, was bathing at Daytona Beach, Fla., on Sept. 4, 1929. A few hours later he began to have intense itching of the buttocks and thighs. This was immediately followed by the appearance of a number of papules which resembled insect bites, to which he applied tincture of iodine. He was first seen on September 23, when he showed large patches of dermatitis from the iodine and many raised linear lesions that were curved or wavy. Some of these had increased in length from ½ to 1 inch (1.27 to 2.5 cm.) in twenty-four hours.

DISCUSSION

DR. WISE: I believe that this patient presents the most extensive eruption of creeping disease exhibited in New York. It resembles the severe cases pictured in Florida by Kirby Smith. I think that treatment with carbon dioxide freezing is the method of choice.

URTICARIA PIGMENTOSA (CHILD). Presented by DR. TRAUB.

A boy, aged 17 months, had an illness that began about one month after birth, with the appearance of yellowish-brown lesions the size of half a dollar, on the skin on the lower left side of the abdomen. During the next five months, numerous similar lesions, varying from 0.5 to 1.5 cm. in diameter, appeared all over the body. Itching was present at no time. Some of the lesions were macular, others were distinctly raised, with yellowish xanthoma-like nodules. Rubbing of many of the lesions caused them to swell and resemble wheals. Biopsy showed an infiltration of mast cells in the corium. The chemical analysis of the blood showed: sodium chloride, 495; sugar, 112.8; urea nitrogen, 14.8; uric acid, 2; cholesterol: whole blood, 147; serum, 188; plasma, 176.

URTICARIA PIGMENTOSA (ADULT). Presented by DR. TRAUB.

A woman, aged 24, unmarried, presented a condition which had started about five years previously at the end of summer, with an eruption of wheals, the size

of a pea, which first appeared on the back of both hands, itched a good deal and, within a few hours or at most a day's time, disappeared, leaving a brownish pigmented area of about the same size as the original wheal. Thereafter, at intervals of a few weeks, she had had repeated similar attacks involving gradually the arms, shoulders, neck, lower extremities and abdomen.

In later attacks the pigmented areas alone became the seat of wheals. Once formed, they did not appear to have changed in color. Itching during attacks was a pronounced feature of this case. Biopsy showed no mast cells in the corium.

The chemical analysis of the blood showed: sodium chloride, 492; sugar, 92; urea nitrogen, 16.5; uric acid, 2.3. The Wassermann reaction of the blood was negative. The basal metabolism was normal.

DISCUSSION

DR. HOWARD FOX: I think that the diagnosis in the case of the child is not easy at first glance. We all know that there is a form of xanthoma in children that closely resembles urticaria pigmentosa. As the lesions became elevated on friction, and as mast cells were found histologically, I agree with the diagnosis of urticaria pigmentosa.

DR. HIGHMAN: I did not see any lesions on the adult that suggested anything in particular, but I suppose the patient has had lesions that made the clinical diagnosis of urticaria pigmentosa. I should like to say a word about the absence of mast cells being adverse to the diagnosis of urticaria pigmentosa. That is not true, and an important piece of work on this subject, by Hartzell, I think published in about 1915, is almost forgotten. I do not see why, because it is an important piece of work. According to him, the absence of mast cells in a given lesion is of no importance as against the diagnosis, since the lesion examined may be a resolving one, so that the absence of mast cells in Dr. Traub's case would not exclude the diagnosis of urticaria pigmentosa.

GRANULOMA ANNULARE. Presented by DR. ABRAMOWITZ.

J. S., a woman, aged 50, from the Post-Graduate Clinic, born in Russia, presented circular and crescentic patches of one year's duration, which were fused together, involving almost the entire radial aspect of the back of the right hand. The back of the left hand showed fewer circular lesions. The lesions were made up of a series of papules the size of a pinhead which were shiny and slightly raised. The centers were entirely clear. At the base of the back of the neck there were isolated lesions, the size of a pea. At the sides of the neck isolated papular lesions were to be seen. A Wassermann test gave negative results. A biopsy had been made but the tissue had not yet been studied.

DISCUSSION

DR. SULZBERGER: I suggest a tuberculin test in this case, because granuloma annulare is supposed to be related to tuberculosis, and belongs to that group of tuberculous diseases which usually gives a negative tuberculin reaction; that is, to those diseases in which the sensitiveness to tuberculin is less than in normal persons. This is considered attributable to a certain degree of immunity which these patients have developed and is called a positive anergy. Substances neutralizing tuberculin have been demonstrated in some of these cases (Fellner, Martenstein, Werner, Jadassohn, etc.). Therefore, if Dr. Abramowitz's case is negative to strong concentrations of tuberculin, this would speak in favor of the diagnosis of granuloma annulare. Of course, all other differential diagnostic measures must be employed.

DR. WISE: I agree with the diagnosis as presented.

DR. FEIT: Although I accept the diagnosis as presented, there are cases which simulate granuloma annulare but belong to the erythema annulare group. (Gray reported such a case.) The lesion in our case, on the back of the hand,

made us first believe that we were dealing with granuloma annulare, but a biopsy showed erythema multiforme. Lesions are observed on the body in granuloma annulare, but do not appear in such a large number in a few days, as in our case.

PAPULONECROTIC TUBERCULID. Presented by DR. PAROUNAGIAN.

Miss R. P., a girl, aged 18, presented a typical example of papulonecrotic tuberculid. The eruption was unusually extensive, involving the forearms, buttocks and legs. Some of the lesions on the legs resembled Bazin's disease. The cervical glands had been excised several years prior to presentation. The eruption had been present, off and on, for two years.

DISCUSSION

DR. HOWARD FOX: I think that all must agree with the diagnosis of papulonecrotic tuberculid as the appearance is classic. For treatment I should suggest a trial with arsphenamine or allied drugs as recommended by Darier. Recently I advised the use of neoarsphenamine in an extensive case of this disease. The patient, a physician's wife, was given a series of thirty-six injections of sulpharsphenamine and at the end of several months the eruption had undergone complete involution. Six months later there was a slight recurrence.

DR. CHARGIN: I have had some experience with the treatment for papulonecrotic tuberculid with the arsphenamines and can state that, in my hands at least, it has not proved to be a satisfactory remedy. Improvement is occasionally noted, but it is neither constant nor lasting.

DR. LANE: I think that there is no doubt that occasionally we get good results in tuberculids as well as in some of the other forms of tuberculosis of the skin from neoarsphenamine. Erythema induratum is frequently benefited by neoarsphenamine. Of course, the results are not invariably good.

DR. PAROUNAGIAN: I saw a patient at the Manhattan Dermatological Society with an ordinary type of papulonecrotic tuberculid, which cleared up under twelve injections of a gold compound, but the lesions returned shortly thereafter. As this case is fairly severe, I think that a gold compound might be tried, and if we do not succeed I shall try arsphenamine later.

PITYRIASIS RUBRA PILARIS OR LICHEN PLANUS? Presented by DR. FEIT.

A girl, aged 7 years, presented a condition of five months' duration, which was generalized, except for the face. She had always enjoyed good health up to the beginning of the present disease, which made her nervous so that she lost a great deal of sleep and about 7 pounds (3.2 Kg.). Nearly the whole integument was covered with a bluish-red, scaly eruption which was slightly raised above the normal skin. The eruption consisted of patches which were made up of polygonal papules that were shiny and showed a depressed center. Some of these papules were arranged in striae, the result of scratching. On the palms and soles there were exfoliation and papules which could be seen more clearly on the stretched skin. The scalp was covered with scales similar to those in psoriasis, but did not give a greasy feeling to the touch like in seborrhea. The nails were not involved. The mucous membrane of the mouth, especially of the cheek, showed a fine lacework of bluish-white papules. There were no plugs on the dorsa of the phalanges. The face was erythematous.

DISCUSSION

DR. POLLITZER: This case impresses me as a good example of a generalized lichen planus. The lesions, where they are discrete, are characteristic of that disease. They run together, forming large sheets, and might create suspicion that we are dealing with a pityriasis rubra pilaris, but in view of the picture presented by the discrete lesions, I do not think that there is any question of the diagnosis; it is a case of lichen planus.

DR. HOWARD FOX: I agree entirely with Dr. Pollitzer and hardly see how there can be any discussion about the diagnosis in this case. It seems to have all the earmarks of a classic extensive lichen planus, even lesions in the buccal mucosa being present. It seems to me that the only interesting point in this case is that it occurred in a child, lichen planus being uncommon in children. According to Kiess, who collected records of eighty cases in children, the disease has been seen in every age from 1 to 15.

DR. FEIT: This case has all the earmarks of lichen planus, but the profuse scaling of the scalp, together with the waxy, masklike expression of the face, suggests Devergie's disease, although the plugs on the dorsum of the phalanges are not present.

TORUS PALANTINUS. Presented by DR. ELLER.

Mrs. N. H., aged 56, born in Ireland, called at the Post-Graduate Clinic on Aug. 12, 1929. She said that she had noted a lump in the roof of the mouth for more than a year, for which she received three radium treatments. On examination there was a raised, smooth, irregularly outlined hard tumor, about 1.5 by 1 by 0.25 cm.

DISCUSSION

DR. TULIPAN: I should like to ask Dr. Eller why radium had been applied to this condition. We know that this is due to a congenital malformation of the bones of the palate, which is practically a normal condition and is often seen.

DR. ELLER: The history states that the patient had received applications of radium before coming to our clinic. The only reason I presented the case is because this congenital anomaly had been mistaken for a pathologic condition and treated.

CAVERNOUS ANGIOMA. Presented by DR. CHEEVER.

S. G., a white man, was normal at birth, but developed the trouble presented when he was a child. He was operated on at the Boston City Hospital many years previously, with some improvement. Examination revealed a colorless, soft swelling of the entire lower part of the face. The tongue was also involved. The patient was presented for therapeutic suggestions.

DISCUSSION

DR. TRAUB: As this case is presented for suggestions as to therapy, I believe that radium should be given first consideration. The result with radium at this man's age will not be as satisfactory as if he had been treated many years ago; nevertheless, with care I believe that his appearance can be much improved. The tongue is particularly interesting because here there seems to be a combination of angioma and lymphangioma, and it is questionable whether much improvement may be expected from irradiation.

DR. WOLF: May I ask in what way Dr. Traub would use radium, whether interstitial or surface application?

DR. TRAUB: I think that that is largely a question of personal experience. Filtered surface applications when large amounts of radium are available certainly will shrink the growth. Owing to the great depth, however, I believe that the method of choice would be needle insertions. The radium is thus placed in close proximity to the tissues on which the greatest action is desired, and the likelihood of damage to the skin or bones is minimized.

DR. WOLF: Great precaution must be taken in treating lesions of this nature with radium because there is danger of producing bone necrosis. In view of the fact that this cavernous angioma is so extensive, one would have to take into consideration the after-effects of the treatment; therefore, in the use of this method

one would have to resort to very small doses. The amount of radium sufficient to obliterate the blood vessels might produce a detrimental effect on the mandible.

DR. ANDREWS: I cannot understand why physicians produce a necrosis of the bone when treating patients with angioma. With modern filtration through platinum and gold there should be no danger. With this method, even when the treatment is given close to the bone, there should be no necrosis. I think, therefore, that Dr. Traub's suggestion is the best, either treatment by radium needles or by filtered implants. I should favor removable platinum seeds.

DR. ELLER: I think that a case in which such large blood vessels are involved would not respond very well to treatment with radium alone. I think that much more favorable results would be obtained by plastic surgery to get rid of the large blood vessels, and then follow up the treatment of the small blood vessels with implantation of radium or treatment with radium from the surface.

DR. HIGHMAN: Has it occurred to any one that it might be a good thing to let well enough alone? The patient's face is not going to be improved very much no matter what we do, and it may be disfigured even more. The results may not turn out to be as successful as we hope they will. If I started that way and were 40 years old, I should keep on.

HYDROA VACCINIFORME. Presented by DR. GROSS.

E. N., a white girl, aged 17, of Swedish-Irish parentage, had been subject to an eruption which made its appearance when she was 7 years old. At that time she suddenly developed a condition around Easter time which was diagnosed as chickenpox. While she was kept at home the condition cleared up but returned immediately on exposure to the sun. Since then the condition had recurred regularly every spring and cleared up around October or November. In the winter only slight attacks occurred when the patient was exposed to the sun in heavy snow. It seemed that the condition had been getting worse every year.

Her mother had died at a young age from Bright's disease. The patient had a twin brother who did not have any skin disease.

On examination the patient presented vesicles and pustules, some of which were umbilicated. On the face, back of the neck, extensor surfaces of the hands and forearms and anterior surfaces of the legs, there were numerous atrophic scars, especially on the face and forearms. On the hands and legs, there were some larger vesicles and lesions resembling furuncles.

SYPHILITIC REINFECTION. Presented by DR. PAROUNAGIAN.

E. M., a man, aged 31, was admitted to the Bellevue syphilis clinic on Oct. 22, 1925, presenting a genital lesion at the frenum (right side), which was of four days' duration. He had been exposed eleven days prior. Even though he had applied mild mercurous chloride to the lesion, the dark-field examination was positive on October 27.

Wassermann examinations made on October 22 and 27 gave negative results. Treatment was instituted on October 29, with applications of arsphenamine and mercuric salicylate, eight of the former and thirteen of the latter. During the treatment, another Wassermann examination was made on Dec. 15, 1925, which also gave negative results. The last injection of mercury was given on June 1, 1926, at which time the patient left town. During his absence, he had no treatment or recurrence.

He returned on Sept. 19, 1929, with two new genital lesions, one on the prepuce and the other in the sulcus to the left side of the frenum. He had been exposed three weeks previously. The first dark-field examination was negative on the day of admission. The Wassermann reaction was also negative on September 19. The dark-field examination made on September 24, however, was positive, confirmed by two of the staff. Another Wassermann test made on September 24 gave a 2 plus reaction.

PHILADELPHIA DERMATOLOGICAL SOCIETY

CARROLL S. WRIGHT, M.D., *Secretary*

Oct. 4, 1929

A. STRAUSS, M.D., *Presiding*

A CASE FOR DIAGNOSIS. Presented by DR. STRAUSS.

A man, aged 20, had a birthmark about the size of a quarter, a brown pigmented mark, which in the last few years had grown to the diameter of a baseball. After hearing Dr. Klauder's paper in Erie on Tuesday, the case struck me as interesting. I should like to have his opinion on it.

DISCUSSION

DR. KLAUDER: This picture of a pigmented nevus, the surface of which is studded with fibroma-like nodules is unusual. I have never seen a similar case, and cannot recall seeing a similar description in the literature. The history of enlargement and the appearance of nodules justify the thought that the condition is malignant. However, I do not believe it is. The long duration from four to six years, the absence of glandular involvement and the fact that the nodules are neither deeply pigmented nor infiltrated are evidence against malignancy. I therefore believe that removal of one of the pediculated nodules for histologic study would be justified. If the patient wants to have the nevus removed, I believe the choice of method should be its entire removal by the so-called radio knife. The lesion should then be studied histologically.

CHROME ULCER. Presented by DR. KLAUDER.

A lithographer, aged 23, had a sharply marginated, indurated, disklike lesion on the web between the second and third fingers of the right hand. The center of its surface presented a red, erosive area. When I first saw the lesion, a tentative diagnosis of chancre was made. There was no glandular involvement. The dark-field examination and the Wassermann reaction were both negative. The patient later told me that he handled chrome. The lesion is shown particularly because it has considerable resemblance to a chancre and the fact that so few cases of chrome ulcer have been shown before the society. One of the illustrations of chrome ulcers in Prosser White's "Volume on Occupational Dermatoses" is a replica of this patient's lesion.

DISCUSSION

DR. STOKES: I am glad to see this exceptionally interesting case. The point that attracted my attention after seeing the lesion on the hand was the patient's nasal septum. He has an ulcer on the right side of the septum and an edema on the left side. It is not yet perforated. Perforation of the nasal septum is characteristic of chrome poisoning in industrial conditions. The patient has complained that his teeth bother him and that his nose is sore.

ERYTHEMA INDURATUM. Presented by DR. GARNER for DR. STOKES.

A colored girl, aged 16, presented herself in July when she had a well developed case of erythema induratum, associated with scars of an old papulonecrotic tuberculid over the knees and elbows. The diagnosis was confirmed by histologic examination. When first seen, the patient presented eight deep ulcers, some of them exceeding 2 inches in diameter. She was given injections of 25 mg. of a gold compound; the dosage was increased to 100 mg. To date she has had ten injections, and the condition is almost completely involuted, with the exception of a small lesion that is still active on the left shin. She is presented to show the result of treatment.

DISCUSSION

DR. STOKES: I think that there is room for investigation of the nonspecific effect of the gold compound, not that I do not think this condition is what we have diagnosed, but because I think this is the effect of gold therapy on presumably tuberculous ulcers of the leg. But pretibial lesions, these chronic septic or traumatic infected ulcers, are often seen in colored people. On obviously nontuberculous lesions, too, the effect may be nonspecific. I believe, however, that this is a therapeutic result in tuberculous ulcers of the leg, and I concur in the diagnosis.

DR. STRAUSS: I agree with Dr. Stokes in what he just said. These patients with papulonecrotic tuberculid improve with any form of protein therapy. I have had the same result with a gold compound as with any foreign protein; the lesions clear up and then there is a severe recurrence.

DR. STOKES: I would not make it as bad as that, but I think it is well to point out the frequency of relapse and the nonspecific character of a good deal of the treatment.

WISE-PARKHURST DISEASE. Presented by DR. CORSON.

P. S., a girl, aged 12, developed an eruption on her scalp, in June after the close of school. It began as one spot, just where, the mother does not accurately recall, and spread steadily over the top of her scalp. She noted that these spongy swellings, globular, some tense and some flaccid, could be pressed on at one place and fluid would ooze out at another. Their appearance was associated with a certain amount of loss of hair over the summits of these elevations, and they presented some inflammatory redness over the same area. There is a decided resemblance to the disease which was described by Wise and Parkhurst as perifolliculitis capitis abdescens et suffodiens. In the scrapings, we seemed to find more spores and mycelial threads than could be accounted for by mere accidental inclusions. No hairs were examined. However, clinically the condition seemed to me Wise-Parkhurst disease.

DISCUSSION

DR. DRANT: I presented a similar case before the society two or three years ago in which the fungus was demonstrated in the hair shafts. In this patient, the condition was healed by the continuous application of hot compresses over a period of several weeks.

DR. STOKES: I am inclined to concur in the diagnosis but I should like to point out that it is, in my opinion, difficult and dangerous to diagnose an eruption on the scalp of this destructive character unless one shortens the hair. Of course, it would be extremely difficult in this case, but if the scalp could be shaved, most astounding configurations might come to light. I think a Wassermann test of the blood would be proper under the circumstances. I agree, however, in the main with the diagnosis that was made, and I agree also with Dr. Drant that hot dressings of potassium permanganate solution applied for long periods of time is the most effective thing, and next to it the coincident application of ointment made of ammoniated mercury. If one can use the roentgen ray and is willing to take chances with it, that is good also.

DR. KLAUDER: I subscribe to the diagnosis.

FACTITIOUS DERMATOSIS WITH UNDERLYING HERPES IN ONE INSTANCE AND PARONYCHIA. Presented by DR. GILMAN for DR. STOKES.

We are showing this woman, aged 30, mainly because of the type of patient she represents, as illustrated by the facies and general make-up. She has a marked psychoneurosis and has been given to certain hallucinations that concerned her scalp. She originally complained of weakness and anemia; the latter could not be confirmed as we found her blood count normal. All laboratory examinations were negative, including the Wassermann test. She has had an eruption on her face

for about six months. She was given treatment together with prolonged interviews. There was some improvement in the result. However, there are still a considerable number of lesions. At one time, she used iodine, but not with the intent of malingering. Her husband is a confirmed drunkard, and is often out of work. They have four children living.

DISCUSSION

DR. CORSON: It would seem to me that latterly, at any rate, her condition comes under the heading of neurotic excoriation, since she applied the iodine not so much with intent to deceive as with the impulse to injure herself.

DR. GILMAN: She is markedly introspective. She had an infestation of scalp lice, and she told us that formerly she noticed that when she cut off certain of her hairs and put them in water they turned into snakes. We convinced her recently, that she had lice and since that time she has been using kerosene and larkspur twice a week. Now, however, she is convinced that she is swarming with lice, although her head is free from them.

PRURIGO MITIS OF THE SUMMER VARIETY. Presented by DR. GUEQUIERRE.

A colored woman, B. W., aged 32, had had the disease as long as she could remember. It came on with the advent of warm weather and disappeared with cold weather. She had three children and was pregnant at the time of presentation, but had had no other pregnancies. The Wassermann test was negative. The red blood cells numbered 3,000,000, the white blood cells, 9,200 and the hemoglobin 55 per cent.

DISCUSSION

DR. CORSON: On questioning her, I find that there is an urticarial tendency. Certain articles of food, such as berries and acid things, seem to bring out hives, and if this person were a child I would have no hesitation in calling the condition lichen urticatus. It is unusual to have it continue to this age.

DR. KLAUDER: I did not see any prurigo nodules. I would regard the condition as pruritus with secondary excoriation.

ST. LOUIS DERMATOLOGICAL SOCIETY

NORMAN TOBIAS, M.D., *Secretary*

Regular Meeting, Oct. 9, 1929

ROBERT H. DAVIS, M.D., *President*

LICHEN PLANUS. Presented by Dr. C. W. Lane for Dr. William Coleman.

S. T., a man, aged 76, presented on the leg a papular follicular pustular eruption, with excoriations from scratching, and crusted lesions. The legs were edematous. On the hands there was a papular eruption, most marked in the palms. On the anterior surfaces of the wrists were violaceous papules with flat tops, and angular bases, with some having umbilications. A few papules had a glistening appearance. The mucous membrane of the mouth, particularly the cheeks, showed a profuse eruption of white dots, streaks and plaques.

DISCUSSION

DR. BROCKELMANN: My diagnosis is lichen planus.

DR. REEVES: I agree with Dr. Brockelmann. The lesions in the mouth and on the hands are typical.

Dr. Brown: I should like to know if the patient showed any improvement under treatment.

Dr. Reeves: We have treated him only a week.

Dr. Davis: I think we all agree as to the diagnosis.

Dr. Lane: Clinicians have reported success in therapy of lichen planus with intramuscular injections of whole blood. Has any one here met with success by using this method?

Dr. Brown: Dr. Tobias said he had had very good results.

Dr. Mook: We tried that many years ago in cases of lichen planus, but never had results that amounted to anything; the lesions only improved temporarily.

Dr. Lane: Has any one been successful in using roentgen rays over the spine as practiced in Europe and as recently reported favorably by Driver?

Dr. Engman: The reaction caused by the roentgen ray is the same as that caused by foreign protein.

Dr. Davis: Do you get the reaction from light or deep doses?

Dr. Engman: It occurs from almost any dose.

Dr. Davis: That may account for the marked improvement you obtain in psoriasis from the use of roentgen rays, but you cannot keep it up forever.

Miliary Lupoid of Boeck. Presented by Dr. C. W. Lane for Dr. William Coleman.

V. S., a woman, aged 36, presented an eruption on the face, ankles, hands and elbows which had been present for the past two years. There was intense itching. The primary lesion was a small red macule around a hair follicle. The color faded on pressure. The numerous macules gave a dusky mottled appearance. Most of the lesions were on the extensor surfaces of the arms, some being pink, others red, and others brownish, and were firm, smooth, elastic, moving with the skin. There were brown pigment spots and areas of atrophy. No lesions showed ulceration, but some showed a fine scaling. Itching was intense, as shown by excoriations from scratching and some crusted papules. Roentgen-ray examination of the chest did not indicate active tuberculosis, but showed semi-active hilar and peribronchial infiltration, slightly more marked on the right side.

DISCUSSION

Dr. Brockelmann: The condition is undoubtedly a granuloma, probably a tuberculid.

Dr. Toomey: From the clinical appearance, I consider the lesions to be miliary sarcoids of the Boeck type. I should like to see a biopsy of the lesions.

Dr. Mook: The lesion belongs to the class of miliary lupoids described by Boeck. They were formerly classified as sarcoids. They have no relation to those of Darier and Rousey. It has the same pathologic structure as tuberculous lesions, that is, giant cells and plasma cells.

Dr. Reeves: It is a granuloma. It may originate from a condition of the blood as a result of toxemia of some kind, not especially due to tuberculosis bacillus. Darier classified all these cases as tuberculids. There has been no section made as yet.

Dr. Davis: The lesion is probably a tuberculid. I believe you all know that Dr. Guy wrote about such a condition that was not due to tuberculosis, but to various proteins. It was interesting to note the circle and half circle formation. I should be glad to accept the diagnosis of Dr. Engman and Dr. Mook, but I believe we should have sections before being sure.

Dr. Mook: The probable explanation of the circinate grouping is that the capillary blood vessels are supplied by larger vessels and distributed in a circinate

anatomic arrangement. When you see a lesion forming a circle, you will find a blood vessel involvement, as is true of circinate syphilis.

DR. DAVIS: In the usual case of tuberculids we do not have circles.

DR. MOOK: Syphilis and tuberculosis cannot be distinguished pathologically by the microscope.

DR. DAVIS: Tuberculids are due to toxemia, not especially a tuberculosis.

DR. TOOMEY: I should like Dr. Mook to describe the difference between the miliary sarcoid described by Boeck and miliary lupoid if he considers them different lesions.

DR. MOOK: Miliary sarcoid is a term for lupoids. In Europe they are much more familiar with tuberculids, as tuberculosis is very common there.

DR. TOOMEY: All of these miliary sarcoids are lupoids. The difference is in the name and size and the end-result. They form miliary necrotic lesions without appreciable elevation and rarely ulcerate.

FOLLICULAR KERATOTIC NEVUS. Presented by Dr. C. W. Lane.

D. K., a woman, aged 22, gave a history of the condition being present since birth. The lesion, which was localized to the right side, had sharp borders in the anterior and posterior midlines. There were numerous lesions in various stages of development; some were reddish and fluctuated, others were covered with brown crusts, some were pouring out a thick yellow pus, and others were depressed and filled with a black central plug. These plugs could be removed with difficulty but could not be dissolved by the ordinary solvents.

DISCUSSION

DR. MOOK: I think that the lesion is a nevus involving the sebaceous glands, forming comedones and sebaceous cysts that become infected and break down. They still belong to the group of keratosis that involve the sebaceous glands. The material expressed does not resemble that of an ordinary comedone; it does not react to acids, but it may have become too hard. It may be keratotic, but not a keratosis.

DR. TOOMEY: The lesion is a nevus of the purely sebaceous gland type. I consider that it could be classified under the designation of group comedones as described by Crocker about 1896, which we all know now to be etiologically a nevus. The abscesses are simply due to secondary staphylococcus infection. The complete zoniform distribution is interesting and is the best developed I have ever seen in a purely sebaceous nevus.

DR. LANE: This is certainly an unusual type of nevus. In reviewing the literature, two cases resemble it closely; one to which White gave the name nevus keratosis follicularis, and in England that which was called nevus acneformis lateralis. The former showed no involvement of the sebaceous glands. The present histologic and clinical picture resembles very closely the condition called nevus acneformis lateralis. The question of therapy is also important. We have advised surgical excision, which the patient refuses. Roentgen therapy is now being considered to attempt to dry up the production of sebum and to reduce the infection.

DR. MOOK: If you give the patient a secondary reaction, it is better to let the lesion alone. You may produce a dissemination in these scars. A large scar later in life may develop carcinoma.

SENILE FRECKLE. Presented by Dr. C. W. Lane.

L. K., a woman, aged 73, stated that about twenty-five years ago there developed an area of pigmentation on the right cheek which spread gradually until the entire cheek was included. It was sharply bordered and irregular in outline. There

was no elevation or depression, nor any subjective symptoms. Two lesions present as two small tumor masses at the time of presentation developed in this area about two years before. The larger one was about 1 cm. in diameter, the smaller one about 0.75 cm. The borders of both were hard, and the larger, after being denuded of its covering and crusts, bled rather profusely. These lesions, after being treated with radium in 1925, disappeared. Later, new nodules appeared just lateral to the outer canthus of the right eye. The patient then presented a marked pigmentation of the right cheek, which involved the upper half and extended to the side of the nose and to the lower and upper right eyelids. As the ear was approached, the color became dark brown. Just below and lateral to the eye were four raised pea-sized tubercules with rough warty surfaces. Biopsy of a small nodule from the face was diagnosed as prickle cell carcinoma with pigment. Biopsy from a specimen of the pigmented area of skin was diagnosed as nevus carcinoma.

DISCUSSION

DR. TOOMEY: In treating these lesions with radium or roentgen rays, there is a very large element of danger. I advise leaving them alone, or better, if possible, removing them radically in toto at the first instance, by clear surgical procedure or the cautery knife.

DR. MOOK: The pathologic slide shows very large black pigmented glands disseminated through the corium three fourths of an inch deep. They might be disseminating now; there is no way that infiltration shows up. It just develops in connective tissue.

DR. DAVIS: I think we all agree as to the diagnosis of black nevus; though it is innocent looking, it is better that we do nothing.

A CASE FOR DIAGNOSIS. Presented by Dr. George D. Reeves.

E. D., a married woman, aged 52, gave a history of a generalized macular chronic dermatitis of fourteen years' duration. The lesions were erythematous, had a tendency to be annular, and were covered with fine branlike scale. The condition had continually progressed. However, there were times when there seemed to be some remission. The patient gave a history of having had several ulcers on the lower limbs. Other than the scaling and associated itching, she had had no untoward symptoms.

On Sept. 14, 1929, the blood count was: red blood cells, 4,400,000; hemoglobin, 90 per cent; white blood cells, 4,800. On Oct. 4, the blood count was: white blood cells, 5,400; lymphocytes, 49 per cent; polymorphonuclears, 41 per cent; eosinophils, 3 per cent. Examination of the urine gave negative results. The biopsy report showed acute inflammation of the corium and localized areas in the epithelium. The Wassermann test was negative.

DISCUSSION

DR. BROCKELMANN: My diagnosis is leukemia cutis, in spite of the nonconfirming blood picture at the present time.

DR. TOOMEY: The blood count did not impress me as high, that is, the percentage was not unusual, although the relative percentage of small cells was high. What impressed me is the fact that the disease had gone on for so long a time (fourteen years) without developing either a more definite blood picture or tumor formation in the skin. I am inclined to look on the condition as parapsoriasis; the patient has had it fourteen years.

DR. GREINER: I thought it might be mycosis fungoides, although it has existed fourteen years, but with the blood picture, I doubt that diagnosis.

DR. LANE: Clinically, this condition appears to be mycosis fungoides and the history of previous tumor formation, which was ulcerated and scarred, seems to bear this out. The histologic picture, however, is that of a leukemia, and the differ-

ential count suggests some leukemic changes. Further study and observation will help to decide, but for the present we can only say it is in the lymphoblastoma group.

DR. DAVIS: I believe that this is a case of mycosis fungoides. I should cling to that diagnosis unless the blood picture shows pretty well that it is a leukemia. In the secondary leukemias I have seen, a leukemia is more of a sheet-like lesion. This type is characteristic of mycosis, and considerable infiltration is present.

DR. TOOMEY: The fact that there is nothing of importance in the blood picture makes me think more of the diagnosis of parapsoriasis. There is not the infiltration of the skin one finds in an old case of mycosis fungoides, nor the bizarre pattern. The itching has been too inconstant, and its seasonal variation is more suggestive of parapsoriasis than a mycosis fungoides.

A CASE FOR DIAGNOSIS. Presented by Dr. George D. Reeves.

A. G., a man, aged 58, gave a history of the condition which began two years ago as a sore spot on the upper gum due to irritation from false teeth. The patient applied several antiseptic solutions, but the condition gradually became worse, involving the entire mouth and lips. He does not smoke nor chew tobacco. The entire roof of the patient's mouth and buccal cavities were reddened with scattered ulcerated areas and white areas anteriorly, and in the inner angle of the mouth. Both lateral and inferior surfaces of the tongue were an angry red, extremely tender and ulcerated with grayish-white patches. Examination on Aug. 15, 1929, showed that the condition was aggravated since the last observation. There were bright gray leukoplakic-like spots on the free borders of the lips. The roof of the mouth and buccal mucous membrane were raw, bright red, and covered with a thin membrane. The process extended down to the uvula. On the hard palate were discrete patches of gray and yellowish-gray, which looked like bacterial colonies. One patch on the lower lip was beginning to look nodular.

Smears showed pure *Staphylococcus citreus,* except for three colonies of white flattened colonies, which was a bacillus. Biopsy showed round cell infiltration and fibrosis.

DISCUSSION

DR. BROCKELMANN: This case was presented as pemphigus at a previous meeting. I do not know if tuberculosis can be ruled out completely.

DR. TOOMEY: I am inclined to hold to the early diagnosis of pemphigus, but have also considered the not improbable fact of its being a chronic low grade Vincent infection.

DR. MOOK: The condition is of from five to six years' duration. The patient has been treated by numerous physicians in the city and by a noted stomatologist for two years, who applied local applications. The condition grew worse and has not improved since we have seen him. Smears have been made for tuberculosis bacillus, but none were found. I think that the condition is tuberculosis of the mouth.

DR. DAVIS: Arsenic was given and the condition began to improve, but in two weeks, the patient began to react badly to the arsenic, so it was discontinued.

DR. LANE: The patient has been under observation for some time, and up to date no diagnosis has been made. When first seen the ulcerations were thought to be due to trauma and medication, as various remedies and cauterization had been employed by other physicians. Later, a Vincent's infection was considered and ruled out. A biopsy showed only chronic inflammatory changes. Laboratory tests have failed to reveal any evidences of tuberculosis and syphilis. Physical examination is normal except for the pathologic process in the mouth. Pemphigus was suggested and the Davis treatment employed with only slight improvement. Any suggestion as to diagnosis and treatment will be appreciated.

PITYRIASIS RUBRA OF HEBRA. Presented by Dr. George D. Reeves.

E. K., a man, aged 70, presented a generalized chronic dermatitis involving the entire body. The condition started about one year ago as a mild eruption under the arm and in the groins. The eruption was accompanied by intense itching. The condition gradually spread to the bends of the elbows, forearms, ankles, knees and abdomen. At the time of presentation the whole skin surface was involved, being covered with a fine whitish scale. The skin was erythematous and thickened. The patient had a generalized lymph adenopathy. The palms were hyperkeratotic and scaly. The blood count on June 4, 1929, was: white blood cells, 8,600; polymorphonuclears, 66 per cent; lymphocytes, 33 per cent; eosinophils, 1 per cent; on June 7: polymorphonuclears, 76 per cent; lymphocytes, 14 per cent; eosinophils, 9 per cent; on June 14: white blood cells, 10,900; lymphocytes, 16 per cent; polymorphonuclears, 72 per cent; eosinophils, 2 per cent; on Aug. 8: white blood cells, 13,600; lymphocytes, 19 per cent; polymorphonuclears, 81 per cent; eosinophils, 9 per cent; on August 28: white blood cells, 9,800; lymphocytes, 26 per cent; polymorphonuclears, 74 per cent, and eosinophils, 8 per cent. Biopsy of the skin showed a subpapillary inflammatory condition (leukemia cutis); biopsy of lymph gland showed marked hyperplasia.

DISCUSSION

DR. STRYKER: This patient was presented for me by Dr. Robert Davis before this society on March 13, 1929 (ARCH. DERMAT. & SYPH., **20**:561, [March] 1929.) At that time the skin condition was almost identical with his present condition. The white blood count was then 7,500 cells per cubic millimeter, with 12 per cent eosinophils and 8 per cent lymphocytes. Apparently, this case is undergoing a slow change in which the white blood count is gradually climbing higher. It will be interesting to have this case presented at a later date so that further observations can be made.

DR. REEVES: Ordinarily in lymphoblastoma the glands are much larger than at the present time, especially those in the inguinal region.

DR. DAVIS: I do not think that the increase in the last count of lymphocytes means anything.

DR. TOOMEY: Pityriasis rubra is the exception in leukemia cutis. Originally, it was considered that the skin lesions were always secondary to considerable leukemic blood changes. Many cases, however, will develop a chronic dermatitis long before showing the blood change. I do not think, however, that one is justified in making a definite diagnosis of leukemia cutis until the blood picture is unmistakably characteristic. Until then, you can only suspect that the patient may develop leukemia. I am inclined to believe that this case is one of pityriasis of Hebra, as a leukemia would otherwise probably be in evidence by now.

EPIDERMOLYSIS BULLOSUS. Presented by Dr. C. W. Lane.

N. T., a young girl, aged 9, was brought to the clinic on June 27, 1928, by her aunt who gave the following history: the child had suffered with this condition since birth. The skin of the entire body had been involved. The face, arms and legs showed bullae of various size from 1 to 2 cm. Some were filled with straw-colored fluid, others were empty and flaccid. The tops of some had been destroyed, leaving superficial red ulcerations. On the extremities on the sites of former bullae, dark chocolate-brown pigmentation was present in irregular patches. Bullae had been frequent between the toes and fingers. There was dystrophy of several toe and finger-nails, and slight deformity around the finger joints. On various parts of the abdomen were scars. A large pigmented area was seen on the chest wall. The back was relatively free from blebs, and judging from the scars, had never been the site of many. Both legs were very much involved, much more so on the anterior surfaces.

A blood picture on July 22, 1928 showed: red blood cells, 4,150,000; white blood cells, 7,800; hemoglobin, 70 per cent; differential count: lymphocytes, 58 per cent;

transitionals, 6 per cent; polymorphonuclears, 34 per cent. Biopsy on July 10, 1928, showed separation of the epithelium from the corium, vaculization in the subepithelial tissue with marked loss of elastic tissue. Cultures from the bullae showed slight growth of *Staphylococcus albus*.

DISCUSSION

All agreed on the diagnosis of epidermolysis bullosus.

A CASE FOR DIAGNOSIS. Presented by Dr. George D. Reeves.

P. P., a man, aged 38, presented a condition which began from five to seven years ago as a small mass on the back of the neck. At first it was only 2 or 3 mm. in diameter, was hard, more or less round, and not painful. The mass slowly increased in size until two years ago, when it was approximately 1 cm. in diameter. It was still hard but not painful. Some time after this the mass began to break down and ulcerated. The surrounding tissue became inflammatory. The patient had never had a pus drainage, but had had some bleeding. The condition progressed rapidly during the past two years, at which time the muscles of the back of the neck began drawing the patient's head backward. Associated with this was a sharp shooting pain radiating from the ulcerated area.

Biopsy showed a low grade inflammatory process.

DISCUSSION

DR. TOOMEY: I am inclined to consider the condition the end-result of an old slowly developing Ludwig's angina of a very low grade of virulence. In this stage it is proper to call it a woody phlegmon, or phlegmon lignon.

CLEVELAND DERMATOLOGICAL SOCIETY

H. J. PARKHURST, M.D., *Reporter*

Regular Meeting, Oct. 17, 1929

J. E. RAUSCHKOLB, M.D., *Presiding*

A CASE FOR DIAGNOSIS. Presented by DR. GAMMEL.

M. B., a German laborer, aged 40, who said that he had not had any venereal disease, presented a paper-like thickening and bluish discoloration of almost the entire glans penis, together with several small areas of telangiectasia. The condition was said to have begun on the prepuce two years previously. The preputial area had improved, leaving the glans involved. There had been no irradiation of any kind.

DISCUSSION

DR. COLE: I have seen about six such cases and feel that the condition corresponds to kraurosis vulvae and may possibly lead to malignancy. I would treat it by electrodesiccation.

DR. NETHERTON: One part of the lesion resembled an early basal cell epithelioma.

A CASE FOR DIAGNOSIS. Presented by DR. COLE and DR. DRIVER.

J. R., a man, aged 50, presented a generalized eruption which was said to have started three years before presentation around the border of an infected appendectomy wound, spreading gradually. It was composed of small bright red venules which tended, in places, to arrange themselves in loops and parts of loops.

There were not many areas of definite purpura. Around the operative scar were several telangiectatic spots, and on the abdomen there were confluent reddish vascular changes. Most of these patches blanched under pressure. In some places there was a suggestion of beginning atrophy, but nothing definite. The biopsy report had not yet been returned.

DISCUSSION

DR. PARKHURST: Apparently the diagnosis lies between poikiloderma atrophicans vasculare and purpura annularis telangiectodes.

DR. FISHER: It looks like a case of angioma serpiginosum.

DR. BARNEY: I favor a diagnosis of purpura annularis telangiectodes.

DR. COLE: We have had the patient under observation for only a few days. If this were poikiloderma, present for five years, there should be more atrophy. Tentatively, I incline toward a diagnosis of purpura annularis telangiectodes.

ACRODERMATITIS CHRONICA ATROPHICANS. Presented by DR. LITTMAN.

Mrs. P. K., a Jewess, aged 61, complained of generalized pruritus of two years' duration, dating from a time when two of her daughters had been treated for scabies. During the entire two-year period she had been applying 10 per cent sulphur ointment. There was a dermatitis, with atrophy, involving the extensor surfaces of the upper and lower extremities, especially the upper.

DISCUSSION

DR. MISKJIAN: This is clearly a case of acrodermatitis chronica atrophicans.

DR. LAROCCO, DR. NETHERTON, DR. GAMMEL, DR. FISHER and DR. COLE agreed with the diagnosis of the case as presented.

A CASE FOR DIAGNOSIS. Presented by DR. NETHERTON.

A girl, aged 16, in good general health, had first noticed rough scaly spots appear on her arms when she was 6 years old. From time to time, other areas had developed on the legs, buttocks and back. The hair growth on the scalp had always been sparse, and there was a follicular hyperkeratosis on the scalp. On the dorsa of the hands and the extensor and flexor surfaces of the arms there were well defined irregular thickened hyperkeratotic plaques. The cubital fossae were slightly involved. There was no apparent inflammatory reaction. The front of the ankles, legs, knees, popliteal spaces and buttocks were also involved, with linear verrucous areas. The patches on the buttocks were large. There were less pronounced, apparently earlier lesions on the midback and neck. There was follicular hyperkeratosis and plugging. No vesicles were found. Many of the nails showed total leukonychia. Histologic slides were presented, showing hyperkeratosis without parakeratosis, and no dermal reaction.

DISCUSSION

DR. COLE: It is hard to classify this case exactly. Among the congenital dyskeratoses or keratodermas are many things. Some may even have bullous lesions. This patient has changes in the hair and dyskeratotic lesions like those in pityriasis rubra pilaris. Some areas resemble those of acanthosis nigricans. This is probabably ichthyosis hystrix, but not a frank case. It may possibly be a congenital acanthosis nigricans.

DR. PARKHURST: The scalp condition looks like monilethrix.

TERTIARY SYPHILID. Presented by DR. COLE and DR. DRIVER.

R. S., a man, aged 23, presented scars over the sternum and nodular and ulcerating lesions on both sides of the neck. The condition had been present since December, 1927, and the lesions had been incised and curetted several times

and treated with roentgen and ultraviolet rays. The Wassermann reaction was strongly positive, and the lesions were healing under the administration of arsphenamines and potassium iodide. There were no physical signs of tuberculosis.

DISCUSSION

DR. PARKHURST: Apparently this is another case of late syphilis in which operation has been performed several times and in which the condition is finally clearing up under antisyphilitic treatment.

A CASE FOR DIAGNOSIS. Presented by DR. COLE and DR. DRIVER.

N. R., a widow, aged 52, had a double palm-sized scar with scalloped border over the left scapula, a result of lesions which had developed two and one-half years previously and had subsided under antisyphilitic treatment. Having received weekly intravenous or intramuscular injections for sixteen months, the patient still presented a positive Wassermann reaction. For fifteen days prior to the time of presentation there had been painful nodules above and below the right ear, on the jaw and on the dorsum of the right hand. These lesions had broken down, and were discharging a bloody yellow material. There were several nodules on the left side of the face and in the left auditory canal.

DISCUSSION

DR. BARRETT: I saw this patient at the Lakeside Hospital Dispensary. Since she said that she had been taking a tonic, I considered this probably an iodide or bromide eruption.

DR. COLE: The condition looks like furunculosis, in a patient with an old syphilitic infection.

DR. BARNEY: Some of the lesions appeared to be granuloma pyogenicum.

DR. MISKJIAN: I feel that this is furunculosis, with some pyogenic granulomas developing.

A CASE FOR DIAGNOSIS. Presented by DR. COLE and DR. DRIVER.

S. W., a negro, aged 26, presented a generalized follicular papular eruption of seven months' duration, with grouping and some confluence on the eyelids, chin, sides of the nose, neck, prepuce, scrotum, buttocks and extremities. There were lesions on the nasal mucosa, and also generalized lymphadenopathy. Roentgenograms of the chest showed signs of extensive fibrous tuberculosis. The Wassermann reaction was strongly positive, and the patient had had two penile sores two years previously. Histologic slides showed the picture of a chronic granuloma, suggestive of syphilis.

DISCUSSION

DR. PARKHURST: The small lesions on the eyelids, neck and extremities have the appearance of miliary tuberculosis.

DR. NETHERTON: I agree with a diagnosis of tuberculosis, although the slides showed no tubercles.

DR. MISKJIAN: The patient has large lymph nodes and moist scrotal lesions. Beside tuberculosis and syphilis, we must consider the possibility of a disease of the lymphatic system. I favor a diagnosis of syphilis, for the lesions are sharply outlined and show corymbriform grouping on the extremities. I found no apple jelly color. He has not received enough arsphenamine to constitute a therapeutic test.

DR. LAROCCO: I consider this a case of miliary cutaneous tuberculosis in a patient with an old syphilitic infection.

DR. COLE: If this is a syphilid, it is unique, for I have never observed one with small pearly nodules like those which appear on the neck. The diagnosis

lies between syphilis and tuberculosis. I feel that the patient has responded to antisyphilitic treatment. The subcutaneous nodules have diminished.

DR. DRIVER: I am unable to say whether this is a syphilitic or a tuberculous eruption.

DR. BARNEY: Some tuberculous processes respond to treatment with arsphenamine.

DR. FISHER: The generalized eruption may be syphilitic, but the facial lesions look like miliary tuberculosis.

DR. BARNEY: The subcutaneous lesions might be sarcoids, fitting in with a cutaneous tuberculosis.

A CASE FOR DIAGNOSIS. Presented by DR. BARNEY.

A. L., a man, aged 78, presented a palm-sized irregularly shaped ulcer on the upper part of the midback, distinctly infiltrated, with an everted, translucent border. It bled easily, and was surrounded by a dull erythematous margin, 1 cm. wide. There was a similar pea-sized ulcer to the left side of this one. The ulcer was of two years' duration, having been preceded for six years by a pruritic, scaling patch of smaller size. A histologic slide was presented. There was no clinical evidence of metastasis.

DISCUSSION

DR. DRIVER: This seems to be either a basal cell or a mixed epidermoid carcinoma.

DR. BARNEY: Should it be excised or coagulated?

DR. COLE: Either form of treatment is effective. These tumors do not respond well to irradiation.

MENINGITIS (SYPHILITIC OR TUBERCULOUS?). Presented by DR. COLE and DR. DRIVER.

C. W., a negro, aged 20, had developed a punched-out, cartilaginous penile ulcer eight weeks before presentation, with bilateral inguinal lymph node enlargement and a series of negative dark-field factors. The Wassermann reaction was strongly positive, and the colloidal gold curve of the spinal fluid was then found to be hypoparetic. Fever followed the first and second injections of arsphenamine, with stupor and signs of meningitis. Before these reactions the spinal fluid had been clear, with a cell count of 20; afterward the fluid was yellow, with a cell count ranging between 565 and 1,580, of which from 65 to 75 per cent were mononuclear cells. Blood and spinal fluid cultures had been negative, and radiographic studies revealed no sign of pulmonary tuberculosis.

DISCUSSION

DR. DRIVER: The spinal process seems to have started before the therapy.

DR. COLE: This is either a tuberculous meningitis or a syphilitic pachymeningitis. Further studies will be required to decide this.

PELLAGRA. Presented by DR. COLE and DR. DRIVER.

T. A., a man, aged 43, had been underfed for a long time due to lack of money, and had lost 31 pounds (14.1 Kg.) of body weight during the last year. He had had practically no alcohol. There had been no diarrhea, but some dementia was present. He was emaciated, and the skin of the hands and feet was dry and reddish brown, with a sharp line of upper demarcation at the wrists and ankles. There were some lesions on the neck and over the sternum, and the throat and pharynx were reddened.

A Case for Diagnosis. Presented by Dr. Cole and Dr. Driver.

W. A., a negro, aged 29, presented an ulcer which had practically destroyed the penis. The lesion had first appeared on the prepuce two years previously, and had extended rapidly during the six weeks before presentation. The Wassermann reaction was negative. No Ducrey bacilli or Donovan bodies had been found in smears, and attempts at autoinoculation had failed.

DISCUSSION

Dr. Rauschkolb: This case may be chronic chancroid, but it is more likely to be granuloma inguinale.

Breast Cancer en Cuirasse. Presented by Dr. Steinberg.

Mrs. M., aged 62, had had five children. About seven years before presentation she had first noticed infiltration in the left breast. This process had extended gradually until six months before presentation and rapidly since that time. The entire breast was involved and more or less adherent to underlying structures. There were many confluent nodules, and the surface was glistening and showed erosions. The regional lymph nodes were not palpable. There had been no loss of weight, and the general health seemed good.

DETROIT DERMATOLOGICAL SOCIETY

H. J. Parkhurst, M.D., *Reporter*

Regular Meeting, Oct. 21, 1929

Arthur E. Schiller, M.D., *Presiding*

Nevus Pigmentosus. Presented by Dr. Valade.

D. H., a boy, aged 6 months, presented a brown line on the cheek, 7 mm. long and from 1 to 2 mm. wide, extending downward from the left outer canthus. It had appeared five days after birth, and the parents had considered it to be a silver nitrate stain due to the use of drops in the infant's eyes at birth. Therapeutic suggestions were requested.

DISCUSSION

Dr. Howard Fox (New York): I would suggest the use of solid carbon dioxide in such a case.

Dr. Stevens: I would advise solid carbon dioxide.

Dr. Van Rhee: I have tried solid carbon dioxide and electrodesiccation in such cases, and consider the former the method of choice.

Schamberg's Disease. Presented by Dr. Troxell.

A. S. C., aged 30, a banker, had first noticed small reddish areas on both shins after exposure to sunlight and weeds in September, 1928. Following this onset, which had apparently been an acute dermatitis, the affected areas had enlarged, with sharply defined reddish-brown macules around the borders and many pinpoint reddish punctae, somewhat resembling grains of cayenne pepper. The central areas, coalescing, had left brownish pigmentation, which had persisted. The Wassermann reaction was negative.

DISCUSSION

Dr. Bartholomew: I agree with the diagnosis of Schamberg's disease.

Dr. Wollenberg: I have seen a similar case in which ulceration developed.

DR. HOWARD FOX: By exclusion, Schamberg's disease seems to be the most likely diagnosis. I did not observe cayenne pepper spots in this case. Dr. Schamberg recently told me that all of his cases had occurred in males.

TUBERCULOSIS CUTIS. Presented by DR. VALADE.

V. B., aged 33, janitress, with a strongly positive Wassermann reaction, had received occasional courses of treatment with mercury, bismuth and the arsphenamines for seven or eight years prior to the time of presentation. About seven years before presentation, and shortly following the institution of antisyphilitic treatment, a dime-sized lesion had appeared on the right cheek. This eruption had extended for two years, involving the nose, cheeks and neck. There were many annular papules of medium size, tending to coalesce, those on the neck being larger. There were easily bleeding ulcers of the nasal mucosa. There was some cutaneous scarring, partly the result of treatment. Histologic sections had been pronounced tuberculous at Harper Hospital and at Ann Arbor. A course totaling 6.5 Gm. of gold sodium thiosulphate had been administered, together with lipoiodine (Ciba), with no apparent effect. Since that time applications of solid carbon dioxide had been used, with gratifying results.

DISCUSSION

DR. PARKHURST: At first the scars were suggestive of lupus erythematosus, but the lesions on the upper lip and the histologic observations confirmed the diagnosis of cutaneous tuberculosis.

GENERALIZED LICHEN PLANUS. Presented by DR. STEVENS and DR. HASLEY.

U. T., a man, aged 32, an Italian, presented a generalized eruption of flat violaceous and brownish papules, of ten months' duration. There were some irregular, scaly patches, especially on the trunk, with loss of hair and with pigmentation. There was some linear arrangement and ring-shaped grouping of the lesions.

DISCUSSION

DR. HOWARD FOX: Some of the patches have the typically violaceous color, some are forming rings, and there is some pigmentation on the penis. Has any one had experience with the spinal roentgen treatment, or with mercuric salicylarsenate?

DR. PARKHURST: I have used the spinal roentgen therapy in several cases, with good results. I have given half-unit doses, unfiltered, and have simultaneously applied roentgen therapy to the worst areas of the eruption. However, there was involution of the eruption in areas not directly exposed. I have used mercuric salicylarsenate, in conjunction with local roentgen therapy for a number of years, and it has seemed to be satisfactory.

DR. SHAFFER: I have used roentgen rays and mercuric salicylarsenate together, with good results, but would prefer to administer arsenic by mouth.

DR. JAMIESON: I have tried spinal irradiation, in doses of 1 unit, filtered, and the outcome has been satisfactory in about half of the cases. I consider it no better than other forms of treatment.

DR. HOWARD FOX: Mercuric salicylarsenate is recommended as being a combination of mercury and arsenic.

A CASE FOR DIAGNOSIS. Presented by DR. BEHN.

W. L., a boy, aged 12, presented pruritic pale nodules on the dorsa of the toes, of six months' duration. They were said to have been present intermittently during the first five months and constantly during the sixth month.

DISCUSSION

DR. WOLLENBERG: This unusual condition may possibly be a complication of hyperhidrosis.

DR. HOWARD FOX: They look like callosities due to ill-fitting shoes. It is most unusual to find them in so young a child.

EXTENSIVE VERRUCAE OF THE ORAL MUCOSA. Presented by DR. STEVENS and DR. HASLEY.

G. P. had first noticed warts in the right corner of his mouth ten years previously to presentation. They had spread slowly, and one year before presentation they had involved the left cheek and tongue. Roentgen and high frequency treatment had been used, with some improvement.

DISCUSSION

DR. HOWARD FOX: This case is extraordinary. I should call it an extensive papillary hypertrophy of the tongue and buccal mucosa, apparently not congenital. We often see one or two such growths, but never so many as in this case.

RADIODERMATITIS FOLLOWING EPILATION BY TRICHO METHOD. Presented by DR. STEVENS and DR. HASLEY.

M. W., a woman, aged 49, presented extensive atrophy and telangiectasia of the face, of nineteen months' duration, which was said to have appeared after a year of treatment by the "Tricho System."

DISCUSSION

DR. BEHN: I have seen two of these cases in the past six months, both with atrophy and telangiectasia.

A CASE FOR DIAGNOSIS. Presented by DR. DOTY.

A woman, aged 35, presented an eruption of twelve years' duration, consisting of erythematous plaques on the nose, cheeks and neck, and more infiltrated lesions on the legs.

DISCUSSION

DR. KEIM: I saw the patient several times at Ann Arbor, where biopsy studies indicated it to be a sarcoid. I cannot recall the exact type of sarcoid.

DR. WOLLENBERG: I saw her seven or eight years ago with typical lupus erythematosus over the nose and cheeks. Later some one gave her a series of treatments with Coley's serum, and after a reaction the lesions faded.

DR. JAMIESON: I saw her after she had left Ann Arbor, and diagnosed the condition clinically as sarcoid. She gives a history of having had different types of tuberculosis in various parts of the body.

PITYRIASIS ROSEA IN A NEGRESS. Presented by DR. SCHILLER and DR. SCHLEGELMILCH.

Mrs. V. P., aged 35, had first noticed a macule on the left shoulder two weeks previously. Subsequently the trunk and thighs had been involved. The lesions followed the lines of skin cleavage and showed scaling. The Wassermann reaction was negative.

DERMATITIS REPENS. Presented by DR. STEVENS and DR. HASLEY.

Mrs. J. T., aged 25, a dental assistant, had first noticed a small blister on her thumb three weeks before presentation. After an incision had been made, many vesicles had appeared on the hands and forearms.

PALMAR AND PLANTAR KERATOSES. Presented by DR. BIDDLE.

W. B., a boy, aged 6, had presented a thickening of the palms and soles two years previously, lasting about six weeks. This condition had recurred three weeks before presentation and persisted, with hyperkeratosis, fissuring and some scaling. No examination for fungi had been made.

LICHEN PLANUS VERRUCOSUS. Presented by DR. WOLLENBERG.

Mrs. M. G., aged 40, born in Ireland, had had an extremely pruritic eruption since March, 1929, on the arms, forearms, hands and legs. There were many angular, flat, violaceous papules and, especially on the hands, a few verrucous areas.

KERATOSIS FOLLICULARIS. Presented by DR. KEIM.

P. W., a student, aged 17, stated that his eruption had appeared first on the back and legs four years previously. One year before presentation, after having gradually extended, the process had become generalized. There had been periodic itching. The general health was good. A strikingly symmetrical eruption of small, reddish-brown papules involved the scalp, trunk and extremities. The individual pupales were minute and follicular. They tended to coalesce in large areas. They were firm and rather superficial, and were associated with slight desquamation. The histologic observations were presented, showing the characteristic "psorosperms."

NEW YORK DERMATOLOGICAL SOCIETY

J. FRANK FRASER, M.D., *Secretary*

Regular Meeting, Oct. 23, 1929

PAUL E. BECHET, M.D., *Chairman*

URTICARIA PIGMENTOSA WITH UNUSUALLY WIDESPREAD LESIONS. Presented by DR. WISE.

P. M., a girl, aged 6, from the Post-Graduate Clinic, was born in this country. The family and personal history were negative. The pigmented lesions first appeared when the child was about 2 months old. Her general health was exceptionally good, she being a robust and well nourished child. She presented a generalized pigmented macular and plaquelike eruption involving the greater portion of the skin and affecting the face and scalp. The lesions varied in size from pea-sized macules and papules to areas over 1 inch (2.5 cm.) in diameter, especially on her back and abdomen. The color varied in different lesions, and even in the same plaque, from salmon-yellow to deep brown. On the neck, the lesions were striped, the stripes extending longitudinally along the sides of the neck. There was a moderate degree of dermographism and urticaria, but itching was of only moderate degree. Therapeutic suggestions were requested.

DISCUSSION

DR. HIGHMAN: Lesions of urticaria pigmentosa disappear spontaneously in adult life. Why treat this child?

DR. MACKEE: I agree with Dr. Highman that in all probability the lesions will disappear spontaneously in the course of time. Injections of calcium might be useful, and the application of roentgen rays and ultraviolet light might be tried, but it is not good practice to use roentgen rays on a young child. If used at all, the rays should be given in fractional doses on one area only, as an experiment.

DR. SAENZ, Havana: There are some reports in the German literature of good results following injections of calcium twice weekly.

VON RECKLINGHAUSEN'S DISEASE (WITH GREAT DEFORMITY OF THE FACE). Presented by DR. ELLER.

A woman, aged 33, from the Post-Graduate Clinic, presented a large tumor-like mass on the left side of the face. The tumor hung down for several inches below the mandible. The mouth on that side also presented large nodules. Scattered over the trunk and arms were numerous nodules typical of those found in von Recklinghausen's disease. The process had been present since birth. The patient's sister and grandmother were similarly affected.

DISCUSSION

DR. WILLIAMS: There is no contraindication to plastic surgery in this case.

DR. MACKEE: The large tumor on the face and those on other exposed parts of the body should be treated surgically. The only objection to this is that the repair is not perfect; there is a tendency for the scars to spread after primary union has occurred.

DR. HIGHMAN: Plastic surgery should be attempted, although the healing may not be satisfactory because the tissue is probably myxomatous and myxomatous tissue may not heal. In this case, however, it is well worth taking a chance. I should like to ask Dr. Eller whether he had roentgenograms taken of the long bones and, if so, whether they showed the presence of bone cysts. This must not be confounded with von Recklinghausen's disease of the bones. Lehman, of the University of Virginia, has done some splendid work on this subject.

CONGENITAL KERATODERMA: SQUAMOUS CELL EPITHELIOMA. Presented by DR. WISE.

W. T., a woman, aged 42, single, from the Post-Graduate Clinic, was born in this country. The family history was negative. The patient's general condition was normal. She presented two different lesions. The feet, hands and forearms exhibited a well defined scaly keratoderma which had been present since birth and which occasioned no subjective symptoms. On the feet, the hyperkeratosis appeared as a thickened, somewhat roughened and scaling dusky red surface, extending to the level of the malleoli, where the lesion became sharply demarcated against the normal skin at the ankles. On the hands and forearms the skin was somewhat less hyperkeratotic and presented a uniform brownish-red scaly surface extending to the elbows, where the line of demarcation was well defined, like the edge of a glove. On the inner surface of the middle of the right forearm was a large fungating squamous cell epithelioma, about 2 inches (5 cm.) in diameter. It was situated on the congenitally hyperkeratotic skin. It began about two years before presentation, and about a year later the original lesion was ablated at the Fordham Hospital, a general anesthesia being used. The growth reappeared a few months later and extended rapidly. The axillary glands on the right side were markedly enlarged and also, to a less extent, those in the left axilla.

DISCUSSION

DR. HIGHMAN: This is an embryonic disturbance, a localized type of ichthyosiform erythroderma.

DR. MACKEE: This is rather more than a congenital palmar keratosis; the forearms are also involved, and there is a nevus unius lateralis on the left leg, also erythema, and subungual hyperkeratosis. The case might be classified as congenital ichthyosiform erythroderma; but a better classification would be congenital keratoderma.

DR. WILLIAMS: This is a developmental anomaly; but too much stress should not be laid on the fact of consanguinity, the only effect of which is to increase the chances that a recessive character may become apparent. There is enlargement of the lymph nodes in both axillae.

DR. SULZBERGER: The variegated colors which the lesions present, the telangiectases, the hyperpigmentation and depigmentation, the hyperkeratoses and the formation of a neoplasm in a rather atypical site brought to mind the thought that we might be dealing with an atypical case of xeroderma pigmentosum, although I would not have ventured this remark had I not been prompted to do so by Dr. Highman. At any rate, it would be interesting to see if photosensitivity and hematoporphyrin can be demonstrated in this case.

LUPUS ERYTHEMATOSUS OF THE SCALP. Presented by DR. BECHET.

A. M., a girl, aged 20, stated that for approximately ten years she had had an eruption on the scalp which had slowly but continuously increased since its incidence. On inspection, a large number of red, scaly, scarred areas, several inches in diameter were seen scattered throughout the scalp; these areas were so devoid of hair as to cause severe disfigurement. The patient had received three injections of gold and sodium thiosulphate, 100 mg. each, once weekly, with no improvement. Two years previously, she had received twelve injections of a gold compound at the Mount Sinai dispensary, with no improvement. Therapeutic suggestions were requested.

DISCUSSION

DR. WILLIAMS: Iodine, either in tincture or in ointment, is sometimes effective in these cases.

DR. MACKEE: I agree with the diagnosis. Iodine may be useful, but the main thing is to continue the injections of the gold compound, with periods of rest, until two or three hundred injections have been given if necessary.

DR. SAENZ: I have observed a similar case in which the use of gold compounds during long periods of treatment was satisfactory. Good results have been obtained with cataphoresis, a 5 per cent solution of potassium iodide being used with a current of from 5 to 10 ma. for about twenty minutes. Regrowth of hairs has been observed in previously bald atrophic patches.

DR. WISE: I agree with what Dr. MacKee has said about the use of gold compounds. I would suggest alternating the injections with an injection of silver arsphenamine.

DR. HIGHMAN: Under the circumstances, the iodine treatment might be tried, but the efficacy of the iodine depends on the administration of quinine internally.

DR. ELLER: In considering local treatment, carbon dioxide snow ought not to be omitted.

DR. BECHET: I am grateful for the therapeutic suggestions. In corroboration of Dr. MacKee's warning not to give up the treatment with gold compounds too soon, I am sure all of you recall an extensive case of lupus erythematosus shown by me at the Atlantic Dermatological Conference held in New York three years ago. The man's face was entirely covered by an inveterate lupus erythematosus of thirty years' duration. This patient is now practically well after a treatment of two and a half years with a gold preparation, and with apparently no deleterious effect on either the kidneys or his general health; on the contrary, there has been a gain in weight and a decided improvement in his general health. I shall persevere with this treatment in the case presented; it is probably the only hope that this young woman has.

LEUKODERMA TREATED WITH AUROTHERAPY FOLLOWED BY DERMATITIS. Presented by DR. BECHET.

A woman, aged 30, presented an unusually extensive leukoderma of several years' duration. The patches were most extensive on the forearms and neck.

In accordance with the suggestions of Lindsay in the ARCHIVES OF DERMATOLOGY AND SYPHILOLOGY for July, 1929, gold and sodium thiosulphate was used. Five injections of the gold compound were given once weekly in 50 mg. doses. A few days after the fifth injection, a severe erythematovesiculobullous eruption supervened on the arms and rapidly spread over the body. There was some fever, and the patient felt sick. The dermatitis at first seemed worse over the depigmented areas, but it soon appeared just as severe all over the body.

The case was presented because of the unusual severity of the eruption, which had proved exceedingly rare among the large number of cases of lupus erythematosus in which the presenter has used this drug.

DISCUSSION

DR. MALONEY: We have used injections of gold and sodium thiosulphate in four cases of vitiligo in doses ranging from 25 to 100 mg. There was some improvement in one case, but none in the other three. My impression is that the cases reported by Lindsay occurred in patients who had been exposed to the sun a good deal. It is possible that this type of case may respond to this treatment or may tend to improve when kept out of the sun.

DR. BECHET: Lindsay states that photosensitivity to the rays of the sun results in hematoporphyrinuria, and that injections of hematoporphyrin cause dangerous sensitivity to the sun's rays. In counteraction to this sensitivity, which he believes is a causative factor in leukoderma, he finds that treatment with gold and sodium thiosulphate decreases this sensitivity to a marked degree, and that he has obtained some good results from its use in this disease. In my experience, dermatitis after the administration of a gold compound has been exceedingly rare; in fact, this is the first severe cutaneous reaction attained, despite its extensive use in lupus erythematosus.

DR. HIGHMAN: Photosensitivity is due to the fact that depigmented areas lack protection against the sun's rays. I cannot see what hematoporphyrin has to do with the question.

DR. SULZBERGER: Bloch claims that pigment never returns to definite vitiliginous areas in which the dopa reaction is negative, as this shows that the pigment-forming faculty is lost, oxidase no longer being present. However, Bushke claims that by irritating these areas new pigment can be induced to form. It is also claimed that one of the best means of irritating such areas is painting with oil of bergamot in alcoholic solution, and the subsequent application of ultraviolet rays. This is the mechanism of the formation of hyperpigmentation in E. Hoffman's berloque dermatitis, and has recently been recommended as a treatment for vitiligo. The recent experiments of Peck in Bloch's clinic seemed to show that in rabbits, pigment is formed only when the irritated areas are exposed to light. Irritation without light does not form pigment. I think that if any beneficial effects are obtained from the use of gold compounds, they must be attributed to the irritation of the skin, as the metallic gold is not a constituent of human melanin.

DR. HIGHMAN: About eight years ago, at a meeting of the New York Dermatological Society, I showed a patient with vitiligo of the neck and shoulders. Suprarenal gland extract and ultraviolet light produced results in some lesions.

LEPROSY WITH UNUSUAL NERVE THICKENING. Presented by DR. WISE.

H. M., a man, aged 23, a native of the Philippines, was a patient at the Post-Graduate Hospital. He had been in this country six months. He first noticed the lesions on his face five months prior to presentation.

He presented six lesions on the face, distributed over the cheeks and glabella: these were oval-shaped, flat, depigmented and slightly reddened, nonscaly, faintly infiltrated macules and plaques. On the forearms were several small depigmented and hyperpigmented macular lesions in stages of involution. Anesthesia and

paresthesia were absent. There was extreme thickening of the ulnar and peroneal nerves, and the posterior auricular nerves stood out prominently in the form of thick strands and nodes. There was also atrophy of some of the muscles of the hands. Subjective symptoms were absent. The search for bacilli in smears yielded negative results, but the histologic examination revealed the structure of leprosy in one of the lesions.

DISCUSSION

DR. SAENZ: Leprosy is prevalent in Cuba. I have observed three cases in which the cervical and occipital nerves were enlarged, not only easily verified by palpation but also by sight, with nodular enlargements and, in the early periods, painful to pressure. This type of neuritis is more often seen in the anesthetic form of leprosy.

CHROMHIDROSIS. Presented by DR. BECHET.

L. R., aged 19, stated that for six months he had noticed red stains on his undershirt at the armpits. An examination disclosed a hyperhidrosis of the axillae. The sweat was brick red; the coloring seemed to emanate mostly from the hairs, which were swollen, irregular and covered by bright red nodules. The undershirt was colored distinctly red. Bacteriologic examination had not been completed. Gram-negative, large, sporelike bodies had been demonstrated.

DISCUSSION

DR. SAENZ: I really think that this case is not one of chromhidrosis. I think that it is due to a fungus that has a predilection for the axillae and produces a condition called trichomycosis palmellina or lepothrix.

DR. HIGHMAN: It is not due to discoloration of the sweat by a metabolic disturbance, but is a local discoloration due to the presence of fungi.

DR. WILLIAMS: Is there any chromhidrosis except sweat discolored by organisms in the hair?

DR. ELLER: As the patient has neurotic excoriations on the face, the sweating in the axillae probably is also of neurogenic origin.

DR. BECHET: Trommsdorff believes that micro-organisms are always present and that they should be regarded as special forms of lepothrix (trichomycosis palmellina, Pick). The hairs are swollen, nodular and brick-red, the changes being evidently due to the invasion of the tendrils by a micro-organism which I personally believe is responsible in all types of chromhidrosis. I do not think it possible, as was formerly believed, that colored sweat can exude directly from the sweat glands; it is the influence of a single micro-organism, or a group of micro-organisms, which is responsible for this disease — which in this particular patient is located in the axillae only. A culture and smear of the organism is being made and will be reported on at a future meeting. The patient has a concomitant acne, which he picks constantly with his nails.

LICHEN PLANUS LIMITED TO MUCOUS MEMBRANE OF THE MOUTH. Presented by DR. TRAUB.

An Italian garage man, aged 30, four to five months prior to presentation began to develop typical papules of lichen planus on the tongue and mucous membrane of both cheeks. There were discrete lesions and coalesced papules forming reticulated areas. The color was mostly white, but there was some erythema. The treatment had been be mercuric salicylarsenate and alkaline mouth wash.

DISCUSSION

DR. SAENZ: In my practice these patients have proved to be refractory to treatment. I observed one patient who did not respond to treatment in eight years; almost every remedy used for the disease was tried without any results whatsoever.

DR. MACKEE: I agree with Dr. Saenz: I have never succeeded in curing a widespread lichen planus of the mouth. The condition does not yield to mercury, arsenic or radium.

DR. WISE: The impression that lichen planus of the mucous membrane of the mouth can be cured only with difficulty is due to the fact that permanent changes take place analogous to leukoplakia, so that it is difficult to differentiate a case in which cure has been obtained from one in which the condition is still active. Two cases with the typical lacework appearance of the buccal mucosa responded with the same degree of rapidity as did the lesions of the skin.

DR. HIGHMAN: There are two groups of lesions of the mucous membrane: one of these accompanies the acute generalized type of lichen planus and disappears rapidly under treatment; the other form, which is chronic, may or may not get well; like the hypertrophic form in the skin, it resists treatment. Dr. Wise's explanation is not tenable, because atrophy looks smooth. I would not treat buccal lichen planus with radium.

DR. RULISON: My experience agrees with that of Dr. MacKee; I consider these cases intractable. Cure may result in time.

DR. BECHET: My experience also coincides with that of Dr. MacKee. A few months ago, I was delighted with the results from a few treatments with roentgen rays given in quarter-unit doses in a severe case of lichen planus of the lips; the lesions disappeared entirely, but in a month or so recurred just as severely.

DR. TRAUB: I should like to emphasize the point made by Dr. Highman in regard to the therapy in these cases. The patients who show lesions of the mucous membrane associated with an acute generalized lichen planus respond promptly to mercury or arsenic, all of the eruption disappearing at the same time. The fixed type of lichen planus, i. e., the cases in which there are a few thickened patches or plaques, irrespective of whether they are on the mucous membranes or on the skin, do not respond well to any type of therapy, but occasionally do disappear if watched and treated conservatively over a period of time. Local treatment in cases involving the mouth should practically be limited to weak mouth washes; certainly, strong applications of acids, roentgen rays, radium, etc., are distinctly contraindicated. This is well illustrated in a young man of 32 years seen recently, who, because of extensive local treatment on an area of lichen planus on the tongue, developed a carcinoma with fatal metastasis.

DERMATITIS REPENS. Presented by DR. TRAUB.

A. N., a student, aged 20, born in this country said that the trouble presented began eighteen years previously on the hands, developing later on the right heel. It persisted on these areas until four years prior to presentation, when active treatment with arsphenamine and some ointment locally, prescribed by the family physician, cleared the foot and most of the eruption on the hands. Owing to the sudden death of this physician, treatment was suspended, and the trouble on the hands became aggravated, the feet remaining well. All laboratory examinations, including that of the spinal fluid, Wassermann test of blood, blood chemistry and culture of pus from the lesions, were negative. Treatment had been practically of no avail. When presented the palms were dry and scaly and the nails were atrophic. Frequently there were exacerbations of a pustular eruption.

DISCUSSION

DR. ELLER: I believe that the condition is due to a trophic disturbance.

DR. HIGHMAN: I feel the same way as Dr. Eller. I do not think that it is a dermatitis repens in the proper sense.

DR. WISE: The case corresponds to Hallopeau's acrodermatitis pustulosa. Dermatitis repens is associated with a peripheral scaling and a peculiar undermining of the scales. Some of the cases of the so-called dermatitis repens are due to fungi.

DR. MACKEE: I agree with the diagnosis of Hallopeau's disease, but psoriasis of the palms often has exacerbations of pustules and inflammation, and between the attacks the palms are dry and scaly as in this case at present. I think, therefore, that the possibility of psoriasis should be considered.

DR. WILLIAMS: I think that this is a case of Hallopeau's disease. The diagnosis of dermatitis repens was based on an article by Sutton, who concluded that Hallopeau's disease is only a variety of dermatitis repens. I never saw a case which I was convinced was dermatitis repens. Cultures were made in this case observed at the Skin and Cancer Hospital, but the only organism found was the staphylococcus. Examinations for fungi were negative. Dr. MacKee's suggestion of psoriasis is extremely interesting. A good many cases of psoriasis present a picture similar to this one, but they do not show the nail changes we see here.

DR. BECHET: I am surprised that Dr. Williams has so infrequently observed the condition described as dermatitis repens, as it is not uncommon. The case under discussion does not resemble it; it lacks the undermined seropustular border covered with loose epithelium, which is so characteristic of dermatitis repens. Dermatitis repens is always moist, while the present eruption seems almost as dry as psoriasis, though I am not suggesting that diagnosis.

DR. TRAUB: The original description by Crocker of a lesion beginning with an injury and lasting indefinitely varies in some respects from the picture presented by this patient. The disease termed acrodermatite suppurative continué by Hallopeau, is believed by Sutton and others to be identical with dermatitis repens and is so classified in the modern textbooks. It was for this reason that it seemed better to present the patient under the diagnosis of dermatitis repens.

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American Medical Association, Scientific Assembly, Section on Dermatology and Syphilology

William H. Guy, Chairman, Jenkins Arcade, Pittsburgh.
Francis E. Senear, Secretary, 55 E. Washington St., Chicago.
Place: Detroit. Time: June 23-27, 1930.

American Dermatological Association

Udo J. Wile, President, University Hospital, Ann Arbor, Mich.
C. Guy Lane, Secretary, 416 Marlborough St., Boston.
Place: Cleveland. Time: 1930.

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